



# **Smoothing the waves of spasticity: the value of personalized monitoring**

Aiming for neap tide by using a  
monitoring approach

Hans Cornelis Johannis Wilhelmus Kerstens



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# **Smoothing the waves of spasticity: the value of personalized monitoring**

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monitoring approach

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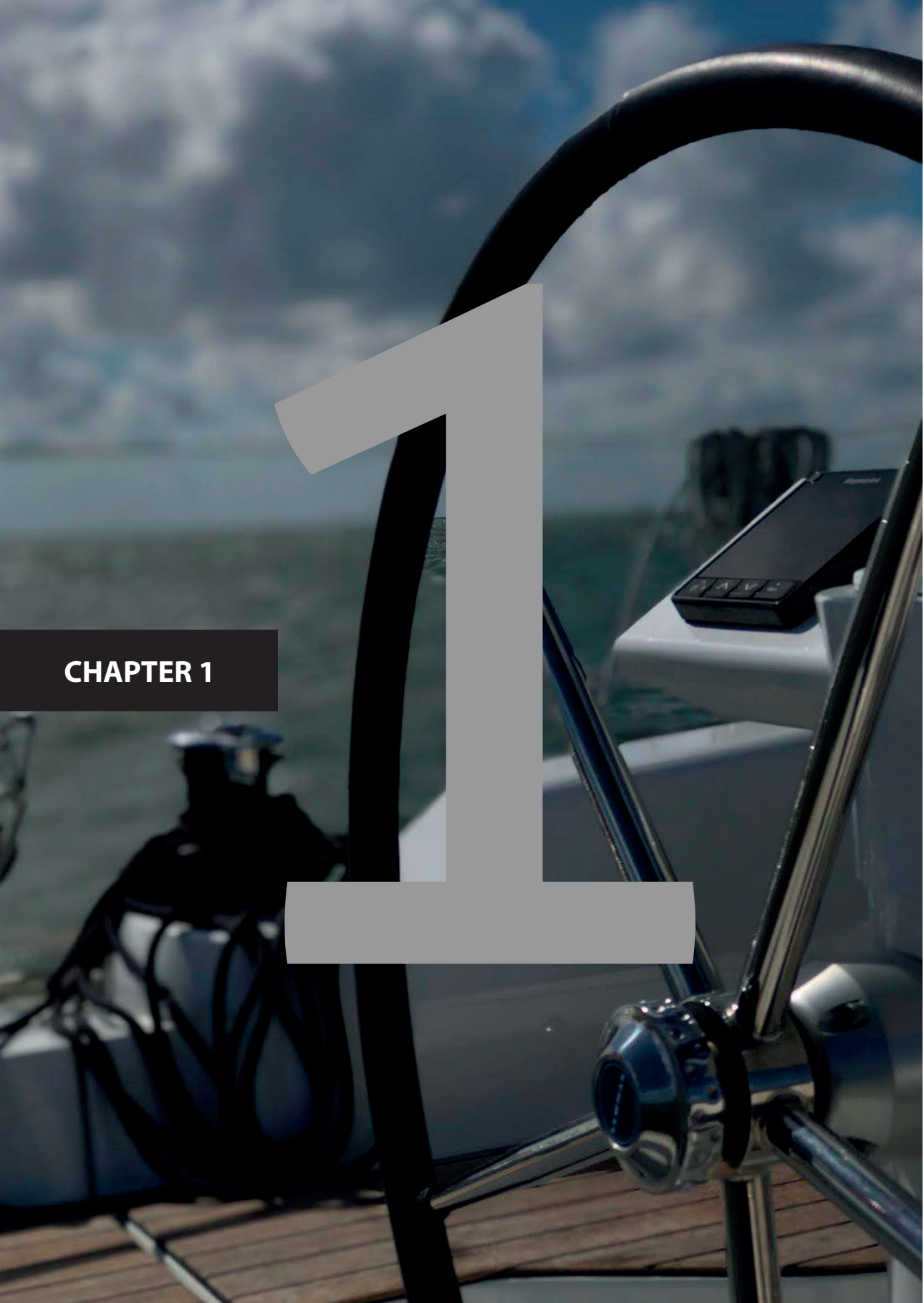






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**CHAPTER 1**

# General introduction



*'Some days I am walking with difficulty, but the next day people see me walking and wonder why is she unfit to work? There is nothing wrong with her. This is very frustrating and difficult to deal with.'*

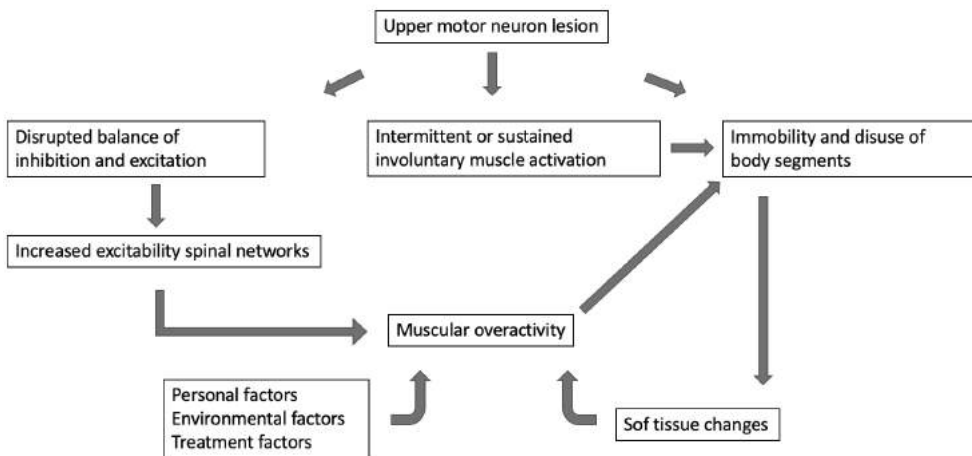
This quote from one of the persons with spasticity who participated in the research presented in this thesis expresses how they have to 'ride the waves' of their spasticity. Instead of mentioning well-known symptoms of spasticity like muscle cramps, stiffness or pain, it emphasizes the impact that spasticity may have on daily activities as well as on employment. It also vents feelings of uncertainty and frustration. Indeed, a person with spasticity continuously needs to adapt to the functional consequences of spasticity, and the daily fluctuations herein, in order to deal with the demands and expectations imposed by the physical and social environment. In my work as a physical therapist, I witnessed this struggle of people with spasticity for almost 30 years, which helped me to formulate the research questions of this thesis, and motivated me to search for answers in an attempt to support patients and their healthcare professionals in proper spasticity management.

People with spasticity wish to 'flatten the waves' to make the level and fluctuations of spasticity acceptable in everyday life. Metaphorically, they are searching for 'neap tide', a situation where the differences between high and low tide are minimal, because the influences from the sun and the moon are acting in opposite directions. Carefully identifying factors influencing spasticity, monitoring the relevant consequences of spasticity, and applying tailored interventions all aim to create such neap tide. Creating a situation of neap tide is, nevertheless, complex because the clinical symptoms and functional impact of spasticity in everyday life vary greatly among individual patients. Moreover, spasticity management requires close collaboration between patients and healthcare professionals regarding the selection, timing, and fine-tuning of interventions to reduce the burden of spasticity. That is why creating neap tide in spasticity management requires patient-centered care. In the optimal situation, the patient is well-informed and equipped to be right in the center of their own treatment team, conducting the team according to his/her needs, and actively participating in shared-decision making on the best treatment approach. Therefore, the aim of my thesis is to improve patient-centered or 'personalized' spasticity management by investigating the experiences and needs of patients with spasticity and by developing and evaluating a monitoring tool feasible for patients, physicians, and allied health professionals. Ideally, this tool should include outcomes that are relevant to patients and be able to monitor the course of spasticity and its functional consequences over time.

## **Spasticity**

Spasticity is a clinical symptom in several disorders of the central nervous system, for example stroke, multiple sclerosis (MS), spinal cord injury, or hereditary spastic paraparesis (HSP). The prevalence of spasticity in these disorders is estimated to be 39-44%,

65-78%, 34%, and 100%, respectively [1-4]. Spasticity has originally been defined by Lance [5] as “a motor disorder characterized by a velocity-dependent increase in tonic stretch reflexes (‘muscle tone’) with exaggerated tendon jerks, resulting from hyper-excitability of the stretch reflex, as one component of the upper motor neuron syndrome.” More recently, spasticity has been re-defined as “disordered sensorimotor control, resulting from an upper motor neuron lesion, presenting as intermittent or sustained involuntary activation of muscles” [6]. This latter definition acknowledges that the ‘excess’ symptoms of spasticity go far beyond the typical increase in muscle resistance in response to fast muscle stretch. It incorporates, for instance, massive flexion and extension responses upon cutaneous stimulation and a variety of symptoms related to abnormal efference from the brain and spinal cord (e.g. associated reactions, pathological co-contractions, spastic dystonia). The reflexive aspects of spastic muscle overactivity are caused by a disrupted balance between inhibition and excitation of spinal reflexes by descending supraspinal pathways, causing increased excitability of the spinal interneuronal networks [7]. The non-reflexive aspects are related to other pathophysiological mechanisms such as a loss of capacity to selectively activate individual muscles, and abnormal intraspinal processing (i.e., persistent inward currents) [8]. Besides reflexive muscle overactivity, intermittent or sustained involuntary muscle activation may lead to immobility, shortening and disuse of muscles. As a consequence, soft-tissue adaptations occur, leading to mechanical (non-neurogenic) muscle stiffness, muscle contractures, and muscle atrophy. These structural muscle adaptations, in turn, may aggravate muscle overactivity, as the maximal muscle compliance with stretch is easier reached, creating a vicious circle of stretch-dependent spastic paralysis [9]. This vicious circle is visualized in figure 1.



**Figure 1:** Vicious circle of spasticity and its influencing factors

The level of spasticity is often not stable, but affected by both gradual changes and temporary fluctuations. First, spasticity may slowly become more severe over the years, for instance, in people with progressive disorders such as HSP or progressive MS; or spasticity severity may gradually subside, for instance in some people with regressive disorders such as stroke. Second, day-to-day or week-to-week fluctuations may occur, which are often related to personal and environmental factors. For example, emotional status (e.g., fear, anxiety), fatigue, pain or intercurrent medical conditions (e.g., urinary tract infection, constipation, ulcers) may temporarily aggravate spasticity. Possible environmental factors that may influence spasticity severity are temperature changes, or demanding and stressful situations [10]. On top of that, some of the available treatments for spasticity may induce week-to-week fluctuations. Particularly the effects of intramuscular botulinum toxin injections slowly wear on and off, which is related to their pharmacological working mechanism (i.e., a slowly induced blockade of neuromuscular junctions gradually compensated for by regrowth of new neuromuscular junctions). In the long run, the effect of several spasmolytic drug treatments (oral spasmolytics, focal intramuscular botulinum toxin injections, intrathecal baclofen administration) may taper off when secondary muscle changes (stiffness, contracture) develop. These latter changes often remain unnoticed by patients or underdiagnosed by healthcare professionals.

The functional consequences of spasticity may be different for each individual as they not only depend on spasticity severity, but also on what a person with spasticity wants or needs to do and on how they cope with spasticity in daily life. For instance, a 'scissoring gait' due to spasticity of the hip adductors has more functional impact on a person who delivers mail 'door to door' compared to a person with a sedentary job in a call center. The International Classification of Functioning, Disability and Health (ICF) is a classification system for the functional consequences of disease [11]. The ICF is a framework to categorize how a disease impairs bodily functions (e.g., muscle strength, sensibility) and/or structures (e.g., bodily integrity) and limits activities (e.g., walking, grooming) and social participation (e.g., work, hobby, sports). In addition, it takes into account how personal and environmental factors may have a positive or negative influence on impairments, activity limitations and/or participation restrictions. Classifying the consequences of spasticity according to the ICF helps to identify and address patient-relevant problems to support spasticity management.

*'I was a mother, a partner and I was Ineke, the employee. I was good at what I did and enjoyed it. In a blink of an eye things changed. My social activities and networks vanished. Now, unwillingly, I am just a housewife. My arm has spasticity, and my leg has a clonus. Walking has become a 'verb', it does not simply happen without thinking. Because of the botulinum toxin injections I do not have to focus as much when walking. Unfortunately, they only work for eight weeks, after that my foot tilts and my knee hyperextends.'*

This thesis will focus on spasticity management in two specific diseases: HSP and stroke. HSP is an inherited, slowly progressive condition that often becomes symptomatic relatively early in life, whereas stroke is an acquired, often symptomatically regressive disorder that becomes more prevalent at higher age. Together, these medical conditions represent two opposites within the clinical spectrum of spasticity.

## **Hereditary Spastic Paraplegia and Stroke**

### ***HSP***

HSP is a group of inherited neurological disorders with an estimated prevalence of two to ten cases per 100.000 persons in Europe. It affects the function of predominantly the long corticospinal tracts and is characterized by progressive bilateral lower limb spasticity and muscle weakness, which may start at infancy. Quite often, patients also show diminished somatosensation (in particular loss of proprioception) in the distal parts of the legs and symptoms of urinary bladder overactivity [12]. In contrast with complex forms of HSP, cognitive symptoms and other motor symptoms such as ataxia and impairments of the upper extremities or speech are absent in the pure form of HSP [4, 13]. In many people with pure HSP, spasticity is the most prominent motor symptom, while leg muscle strength is relatively preserved [4].

### ***Stroke***

Worldwide, stroke is the second leading cause of death, and third leading cause of disability-adjusted-life-years lost [14]. It occurs from a suddenly impaired cerebral circulation. The reduced blood flow induces a loss of neurological function, which may cause a variety of symptoms, impairments and activity limitations. In addition to cognitive and emotional impairments such as aphasia, apraxia, neglect, and anosognosia, unilateral sensorimotor impairments frequently occur like hemianopia, hemiparesis and hemihypesthesia. The more severe the hemiparesis, the greater the chance of concomitant spasticity in the upper and/or lower extremity [15].

The main differences in the clinical presentation between Stroke and HSP are described in Table 1.



**Table 1:** Differences in clinical characteristics between HSP and stroke

	<b>Stroke</b>	<b>pure HSP</b>
Onset	Sudden	Slowly progressive
Age of onset	Mostly at older age	Mostly in childhood, adolescence, or early adulthood
Inherited	No	Yes
Location of spasticity	Unilateral (upper and/or lower extremity)	Bilateral (lower extremities)
Course of disease	Relatively stable	Progressive
Cognitive impairment	Possible	Unlikely
Presence of spasticity	About 40%	Almost 100%

### Current spasticity management

Spasticity management aims to stabilize or reduce the severity of spasticity and its functional consequences. A variety of pharmacological, non-pharmacological, and surgical interventions can be applied to reduce reflexive and non-reflexive muscle overactivity and mediate possible soft-tissue adaptations [16] (see table 2).

Pharmacological interventions either have a focal or systemic effect on spasticity. Focal injections are possible with botulinum toxin type A (BoNT-A) in spastic muscles, or with phenol or alcohol around peripheral nerves innervating spastic muscles (i.e., chemical neurolysis). Systemic therapy by oral medication is primarily indicated for reducing multi-segmental spasticity. Because oral medication frequently causes side-effects, such as drowsiness or fatigue [17-19], cyclical intramuscular BoNT-A injections are considered and applied more and more, especially when the aim is to reduce focal or segmental spasticity and/or to improve motor control [20]. Indeed, the side effects of BoNT-A are relatively mild and less frequent compared to those of oral medication [18]. When a systemic effect is aimed for and side effects of oral medication limit their application, intrathecal baclofen therapy (ITB) is an alternative option, particularly when widespread spasticity is troublesome in the lower more than the upper extremities.

Non-pharmacological interventions can be categorized in three categories, namely muscle stretching techniques that aim to increase soft-tissue extensibility; physical modalities (e.g., extracorporeal shockwave therapy / ESWT) that aim to restore muscle balance and/or increase soft-tissue extensibility; and surgical procedures. [21, 22] Surgical procedures aim to restore muscle balance around joints, reduce joint deformity, and improve joint stability to improve motor control. Neurectomy procedures focus on reducing disabling muscle overactivity, whereas tendon and joint procedures aim to restore muscle length and create optimal biomechanical preconditions for motor control [23, 24]. Within each of the categories of non-pharmacological interventions, different treatment options are available (see for a detailed overview Table 2).

**Table 2:** Overview of interventions for spasticity and their aims

<b>Intervention category</b>	<b>Aim and type of intervention</b>
<b>Pharmacological agents</b>	<b>Reduce muscle overactivity and reduce related symptoms</b>
Intramuscular botulinum toxin injections	Focal reduction of spasticity by intramuscular blockade of extrafusal and intrafusal muscle fibres
Perineural phenol or alcohol injections	Focal reduction of spasticity by chemical neurolysis (demyelination and axonal degeneration)
Oral medication	Systemic reduction of spasticity (various mechanisms)
Intrathecal baclofen therapy (ITB)	Spinal inhibition of muscle reflexes (GABA-ergic)
<b>Muscle stretching</b>	<b>Increase soft-tissue extensibility and decrease reflex threshold of muscles</b>
Active	Patient initiates and maintains stretching exercises
Passive	Therapists or caregivers support stretching exercises
Prolonged positioning	Prolonged stretching by maintaining a certain sitting or standing position
Casting / splinting	Prolonged stretching by using casts or splints
<b>Physical modalities</b>	<b>Reduce muscle overactivity, restore muscle balance, and increase soft-tissue extensibility</b>
Shockwave	Shockwaves applied as a sequence of single sonic pulses
Ultrasound therapy	Mechanical vibration at 1 or 3 megahertz
Cryotherapy	Applying cold
Thermotherapy	Applying heat
Vibration	Vibratory stimulation
Electrical stimulation	Electrical stimulation of sensory nerves or dermatomes
Neuromuscular stimulation	Electrical (motor) stimulation of muscles
Electro-acupuncture	Applying electric current by acupuncture needles
Transcranial direct current stimulation (tDCS)	Low-current neurostimulation of the cortex at the scalp
Transcranial magnetic stimulation (TMS)	High-output magnetic stimulation of the brain through the scalp
<b>Surgical procedures</b>	<b>Restore muscle balance around joints, reduce joint deformity, and improve joint stability</b>
Tendon procedures	Tenotomy, tendon lengthening, tendon transfers
Joint and bone procedures	Arthrodesis, arthrolysis, osteotomy
Neurectomy procedures	Peripheral neurectomy, selective dorsal rhizotomy

## Challenges in managing spasticity

Although the overview of spasticity interventions presented in Table 2 can be relatively easily compiled from scientific literature, spasticity management ‘in real life’ is much more challenging because patients with spasticity vary greatly in terms of underlying disorders, co-morbidities, patterns and severity of spasticity, and related functional limitations. Moreover, patients prioritize different treatment goals and have different views on which treatment burden they are willing to accept. In the last decade, organization of healthcare has moved toward patient-centeredness, which ultimately implies shared-decision making, shared goal-setting, and self-management. Patient-centeredness has the potential to add value to healthcare, because it does not primarily focus on the symptoms of an illness, but on the needs and values of the individual patient [25]. In shared-decision making, a well-informed patient and well-prepared professional give direction to a treatment plan together, based on shared goal setting [26]. Self-management refers to the way how patients deal with their disease, its functional consequences, and with the emotions, lifestyle and role changes caused by the disease [27]. Patient-centeredness offers a great opportunity to achieve lower healthcare costs in particular within patient populations with a chronic condition. Considering spasticity management, moving toward patient-centeredness creates three key-challenges that are addressed below.

*‘My former physician did not know how to treat my spasticity, explaining I should learn to live with it. My current physician listens. He starts a dialogue and talks with me, unlike others who only read my patient file.’*

First, when aiming for patient-centered care, **spasticity needs to be measured with outcomes that are relevant to patients in order to capture the functional impact of spasticity and to adjust individual treatment plans.** Patient-reported outcomes (PROs) have the potential to quantify the impact of a disease as perceived by patients themselves, and may help to move toward genuinely patient-centered care [28]. However, existing measures of spasticity focus on muscle tone or related impairments such as active or passive joint range of motion. Consequently, there is little knowledge about which PROs are useful and valid for spasticity management in people with stroke or HSP.

Second, disentanglement of structural changes in spasticity severity and temporary spasticity fluctuations is hardly possible, which makes it difficult for patients and healthcare professionals to interpret ad hoc outcomes of a clinical interview or clinical examination. Hence, the challenge is **to systematically sample individual data over a prolonged time period to be able to differentiate between structural and temporary changes in spasticity, either occurring as an effect of time or induced by treatment.**

The third challenge is to incorporate **shared-decision making, shared goal setting, and self-management in regular spasticity management**. Williams et al (2014) found that lack of knowledge and self-efficacy of patients were significant barriers for striving toward shared-decision making and shared goal-setting. Patients should be provided with adequate information and support to interpret the information in order for them to experience that they have influence on the decision-making process [29]. It is well known that patients who are able to participate in 'managing their health' show better outcomes [30]. In this perspective, measuring patient-relevant outcomes (challenge 1) and monitoring these outcomes over time (challenge 2) are prerequisites for dealing with the third challenge (shared-decision making and self-management). It can be questioned, however, whether all patients have the capability to self-manage their health, and whether all healthcare professionals are able to provide adequate information and support to optimize the self-management of their patients [31].

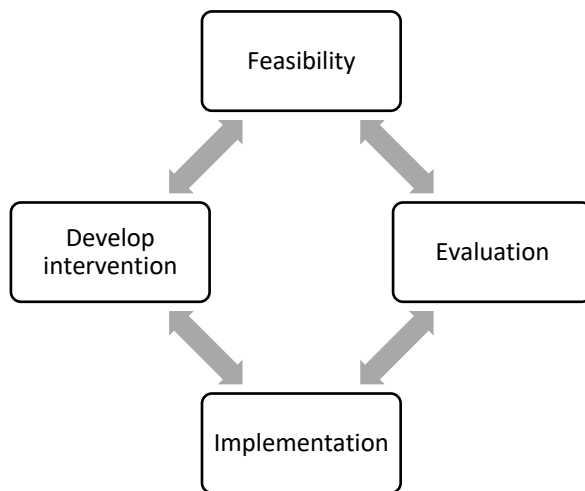
### **Measuring and monitoring patient-relevant outcomes in personalized spasticity management**

In a person-centered approach to spasticity, Turner-Stokes et al (2018) stated that the patient should be at the center of care, and that shared goal setting and evaluation should be key in a spasticity management program. Moreover, they argued that patients (and their caregivers) should be empowered in the application of guided 'self-rehabilitation', which implies that therapists primarily adopt a coaching role to support patients in performing their exercises [32]. It has been argued by Archer et al. that online support may greatly help people with chronic conditions to self-manage their disease if PROs are used, communication between stakeholders is facilitated, online support is easy to use (if necessary, with help of caregivers), and individual barriers to this support are known and dealt with [33]. As such, an effective online tool to support spasticity management can be regarded as an intervention itself, particularly if it includes patient-relevant outcomes covering all relevant levels of the ICF. It should also be easily applicable over prolonged periods of time to detect changes in health status. Furthermore, it should contribute to providing knowledge to the rehabilitation team and empower patients to engage in shared decision-making and goal setting. In other words, an optimal online monitoring tool may greatly support self-management of patients as well as collaboration between professionals and patients.

### **Developing an intervention for personalized spasticity management**

Developing and implementing an online monitoring tool to create personalized spasticity management is complex due to multiple factors, such as the expertise and skills of the patients receiving the intervention, the variability of treatment outcomes, and the number of persons and institutions involved in delivering the intervention [34]. This thesis uses the 'Medical Research Council Framework for developing and evaluating complex

interventions' (MRC framework) to develop and test an online spasticity monitoring tool. The MRC framework follows a systematic approach in which an intervention is developed and tested for feasibility before it is finally implemented at a larger scale [34]. The four phases of this approach are depicted in figure 2. In this thesis, two phases of the MRC framework are addressed, namely, the development and feasibility of an online spasticity monitoring tool. In the development phase, patients' experiences and needs are explored. Based on the experiences and needs of relevant stakeholders, supported by the literature, a prototype of the intervention is developed. In the feasibility phase, the prototype intervention is refined and tested for its feasibility. Evaluating (cost-) effectiveness and a broader implementation of the developed intervention (phase three and four of the MRC framework) lie beyond the scope of this thesis, but some future perspectives will be discussed in the general discussion of this thesis.



**Figure 2:** Phases of the MRC framework for developing and evaluating complex interventions

### **Objectives and research questions of this thesis**

To create neap tide in spasticity management, both patients and healthcare professionals have to deal with many tidal factors that influence the individual clinical presentation and impact of spasticity. Therefore, the objective of this dissertation is to support personalized spasticity management by developing an online monitoring tool that is feasible and useful for patients and healthcare professionals, and that incorporates patient-relevant outcomes. The ultimate goal is to create neap tide for patients with chronic spasticity through implementation of this monitoring tool in their spasticity management. In this context, the following research questions are addressed:

1. How do two different populations (people with HSP and people with stroke) experience their spasticity and its functional consequences in everyday life, and which outcomes of spasticity (treatment) are relevant according to these people?
2. What are the experiences of people with HSP or stroke with current spasticity management?
3. How feasible is it for people with HSP or stroke to monitor their spasticity using an online tool?
4. To what extent does online monitoring provide relevant insight in the course of spasticity to both healthcare professionals and people with HSP or stroke?
5. What barriers and facilitators do people with HSP or stroke and their healthcare professionals perceive when using an online spasticity monitoring tool?

### **Dissertation outline**

This dissertation comprises scientific publications that reflect the five research questions mentioned above and that comprises the two phases (intervention development and feasibility) of the MRC framework for developing and evaluating complex interventions, as a first step to improve personalized healthcare for patients with chronic spasticity.

*Chapter two* contributes to development of the intervention by addressing the first and second research questions. It is a qualitative study describing the experienced impact of spasticity on physical activities, social participation, and well-being amongst people with HSP living in the Netherlands. In addition, interview data are reported regarding patient-relevant outcomes, perceived (un)met needs in current spasticity management, and suggestions for how to meet these (un)met needs.

*Chapter three* is based on the results of an online questionnaire (survey) in the Netherlands and further addresses the first research question. It reports the experienced complaints, activity limitations, and loss of motor capacities in people with HSP.

*Chapter four* is based on the same survey and contributes to the development of the intervention by addressing both the first and second research question with a focus on healthcare needs, expectations, utilization, and experienced treatment effects in people with HSP.

*Chapter five* reports a qualitative study amongst persons with stroke that presents the experienced consequences of chronic spasticity, the experienced effects of botulinum toxin injections, relevant outcomes suggested by patients, and their perceived (un)met needs regarding spasticity management. Hence, it addresses both the first and second research questions.

*Chapter six* is a feasibility study testing the introduction of an online spasticity monitoring tool amongst people with HSP or stroke and their healthcare professionals. It addresses the research questions three, four, and five. It reports pilot results in terms of feasibility and usability, discusses to what extent this tool can provide insight in the course of spasticity, and investigates which barriers and facilitators are experienced when using the tool.

In *chapter seven*, the main findings of this thesis will be discussed and directions for future research will be given.

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**CHAPTER 2**

# The perspective of patients with HSP on spastic paresis

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## **Stumbling, struggling, and shame due to spasticity: A qualitative study of adult persons with hereditary spastic paraplegia**

### ***Purpose***

Little is known concerning the impact of chronic spasticity on physical activities, social participation, and well-being, and whether patients' needs are addressed by current treatments. This study aims to investigate these lacunas in persons with a pure form of hereditary spastic paraplegia (HSP), in whom spasticity is a prominent symptom.

### ***Methods***

Fourteen patients with a pure form of HSP were interviewed. These interviews were recorded, verbally transcribed, and thematically analysed.

### ***Results***

Four themes were identified which can be reflected by the phrases: (1) 'I stumble'; (2) 'I struggle'; (3) 'I feel ashamed'; and (4) 'I need support'. Balance and gait problems led to limitations in domestic activities, employment, and recreation. 'Stumbling' also occurred due to pain, stiffness, and fatigue. Struggling was related to the continuous need for adaptation strategies, including the abandonment of some activities. Participants further reported feelings of shame, fear, and frustration. Lastly, they needed more support in daily activities than currently provided.

### ***Conclusion***

Besides treating spasticity-related motor impairments, patients with HSP need practical support for optimising their physical activities and social participation. They also seek attention for the non-motor consequences of their chronic spasticity to improve their well-being. Patient-reported outcomes might help to address these needs.

Keywords: hereditary spastic paraplegia, spasticity, patient reported outcomes, patient generated health data, qualitative research

## Introduction

Dealing with the consequences of spasticity in daily life is challenging [1]. Current treatment focuses on reducing spasticity-related motor impairments and preventing secondary consequences [2]. A diversity of pharmacological, surgical, and physical interventions aim to reduce muscle tone, restore muscle balance across joints, and prevent secondary muscle changes, such as contractures [2-5]. Mainstay pharmacological treatment is either systemic (oral medication or intrathecal baclofen) or focal (e.g., intramuscular botulinum toxin injections). Besides pharmacological treatment, physical therapy may reduce the biomechanical consequences of spasticity, for example through muscle stretching exercises, (serial) casting, and learning to optimise the performance of activities [5].

The effects of the interventions mentioned above are commonly assessed with outcome measures at the physical impairments level [6], in particular with scales for muscle tone and measures of passive and/or active range of motion [7]. However, such outcomes do not assess the impact of spasticity on physical activities, social participation, or general well-being in persons with spasticity [3]. As a consequence, it is likely that the current medical treatment strategies, traditionally established by healthcare professionals, do not address all the needs and priorities of persons with chronic spasticity.

The primary aim of this study was to investigate how chronic spasticity impacts on physical activities, social participation, and well-being. The secondary aim was to identify whether patients' needs are adequately addressed by the current intervention strategies. In this study we focus on persons with a pure form of hereditary spastic paraplegia (HSP), who experience chronic, progressive spasticity of the lower limbs as their most prominent symptom. Leg muscle strength in these patients is relatively well preserved, probably because the reticulospinal descending tracts are able to compensate for the progressive axonal degeneration of the corticospinal tracts [8]. In addition, sensory deficits are usually mild and cognitive impairments absent [9]. Hence, investigating the impact of chronic spasticity in persons with pure HSP provides an opportunity to study the consequences experienced by and treatment needs in persons with 'relatively isolated' lower-limb spasticity.

## Materials and methods

### Design

A qualitative study was conducted between autumn 2015 and December 2017. A social constructivist epistemology was used in interactions with the interviewer to explore multiple perspectives of the realities perceived by patients with HSP [10]. Using this approach, the experiences of persons with HSP were interpreted with attention to the consequences of chronic lower-limb spasticity for physical activities, participation, and well-being, as well as to the needs of patients. The study was conducted using semi-structured interviews.

## Participants

The participants were persons who had an established diagnosis of autosomal dominant HSP and who had a pure phenotype. Other inclusion criteria were being 18 years of age or older and having had spasticity for more than two years. One exclusion criterion was an inability to communicate in the Dutch language. For the inclusion of participants, purposive sampling was used [10]. This sampling method aims to capture the diversity of experiences and needs within the HSP population, which means that participants were selected to represent the target population regarding personal characteristics such as age, sex, severity of paraparesis and spasticity, and with regard to referral from different sites across the country. Participants were recruited from the database of the outpatient clinic of the department of Rehabilitation of the Radboud university medical center (Radboudumc) between 2014 and 2017. The Radboudumc is a nationally recognised centre of expertise for HSP in the Netherlands. The rehabilitation physician at the Radboudumc contacted persons with HSP by telephone. If the person with HSP was willing to participate, information about the study was sent by email. If the person decided to participate, he or she was asked to contact the researcher by email. The primary researcher (HK) checked both the inclusion and exclusion criteria before an appointment for the interview at the participant's home was planned. All participants gave written informed consent prior to the interview. The local medical ethics committee approved the study protocol (registration number 2015-2121). All data were stored and reported in conformity with the Declaration of Helsinki [11].

## Data collection

An interview guide was developed by the primary researcher (HK) and pre-tested among physiotherapy students for feasibility and length among physiotherapy students. The guide was not used as a strict checklist, but merely as a guideline (see Supplementary material) to ensure completeness at the end of each interview [10]. The one-hour interviews started with open questions to gather information regarding spasticity and its experienced consequences. The in-depth questions focused on the impact of spasticity on physical activities, social participation, and well-being. Subsequently, the interviews focused on patients' reflections on the experienced benefits or adverse effects of the interventions they had received, and whether they felt that these interventions had been adequately tailored to their problems and needs. Next, the interviews explored patients' wishes and ideas about optimal spasticity management with a focus on the solutions they brought up themselves. The results of previous interviews were used to guide the interviews with subsequent participants. The interviews were digitally recorded, and during the interviews, key messages from the participants were written on sticky notes that were attached to a poster. These notes supported the conversations and enabled participants to verify the content obtained during the interviews. The poster with attached sticky notes was photographed to support the analysis after the interview. All interviews

were conducted by the primary researcher (HK), a male physiotherapist with more than 20 years of clinical experience in the rehabilitation of patients with spasticity, including patients with HSP. All interviews were conducted at the participants' homes and two research assistants (physiotherapy students) provided support. These assistants registered the additional field notes and transcribed the audio recordings of interviews verbatim.

Data from the previous interviews was analysed before the next interview was planned. The interviews were stopped at the point when new information no longer came up, in other words, when the collected information reached saturation [12]. To guaranty anonymity, personal details were removed from the interview transcripts and a unique numeric code was assigned to each interview before storing it. The key to identifying individual patients was stored in a separate data folder accessible only by HK.

### **Data analysis**

The interviews were analysed according to the principles of thematic analysis of Braun and Clarke (2006) [13]. The steps in this analysis comprise familiarising oneself with the data, generating initial codes, searching for themes, reviewing themes, and defining themes [13]. The analysis followed an inductive approach without using any previously constructed framework for possible codes.

The principal investigator (HK) coded the first transcript and then discussed the coding process and initial codes with the subsequent coders (DV and TS), both experienced qualitative researchers. After consensus was reached, HK coded the second interview and, once again, discussed it with DV and TS. Again, after agreement was reached, HK coded the remaining interviews. TS peer-reviewed the procedure and the content of the analysis. The codes were compared, checked for overlap, and discussed until a consensus was reached.

During the next step, HK searched for themes by clustering the codes into potential themes. This clustering was supported by consulting the sticky notes attached to the posters. The clustering was discussed with TS until agreement was reached. After reviewing and defining themes, HK, TS and all other authors discussed the themes in three rounds until all approved the final themes. Data were analysed by using Atlas.Ti version 8.1.27.0 (Scientific Software Development GmbH, Berlin, Germany).

### **Trustworthiness**

We used the COREQ criteria for reporting qualitative research [14]. To ensure trustworthiness, the concept credibility (do the data and procedures address the intended focus, and do the themes cover the data?), dependability (do the data change over time?), and transferability (can the results be transferred to other settings or groups?)



[15] were considered in a number of ways. Credibility was taken into account through purposive sampling. We aimed to sample a rich variety of experiences, and therefore included participants with different characteristics, for example, male and female, young and old, employed and unemployed. We presented the conversation notes to each of the participants so that they could check the accuracy. In addition, the principal investigator (HK) discussed the codes with DV and TS, and later in the process with all the researchers. Dependability was assessed using a pre-tested interview guide that was adapted according to the results of the previous interviews, to ensure that similar relevant topics were discussed in the subsequent interviews. To ensure transferability, the participant characteristics were described as well as the process of data collection and analysis.

## Results

A saturation point for new information was reached after 11 interviews. To optimise credibility, we stopped including new participants after 14 interviews. In total, 15 patients with HSP were invited to participate, of whom one person refused due to personal circumstances. A caregiver was present during two of the interviews. The 14 participants comprised a heterogeneous group based on sex, age, marital status, employment, HSP subtype, disease duration, and on whether they had received regular physical therapy (see Table 1). Data analysis led to the identification of four themes that could be reflected by the phrases: (1) *"I stumble"*, (2) *"I struggle"*, (3) *"I feel ashamed"*, and (4) *"I need support"*. Each theme will be elaborated and supported by quotes from the participants.

**Table 1:** Participant characteristics

Participant	Sex	Age	Marital status	Employment	HSP Genotype	Disease duration	Regular physical therapy
1	Male	72	Single, children	No	SPG4	>20 years	Yes
2	Female	50	Single	No	SPG31	>20 years	No
3	Female	56	Cohabitant	No	SPG31	>20 years	No
4	Female	58	Married, children	Yes	SPG31	>20 years	Yes
5	Male	64	Married	No	AD-HSP	>20 years	Yes
6	Male	26	Single	Yes	SPG4	>10 years	Yes
7	Male	48	Married, children	No	SPG4	>10 years	No
8	Male	50	Single	No	SPG4	>10 years	Yes
9	Male	49	Cohabitant	Yes	SPG4	>20 years	No
10	Male	44	Cohabitant	Yes	AD-HSP	>35 years	Yes
11	Female	51	Married, children	Yes	SPG4	>6 years	No
12	Female	53	Married, children	Yes	SPG4	>18 years	No
13	Female	51	Married, children	Yes	SPG10	>4 years	Yes
14	Female	66	Married	No	SPG4	>20 years	Yes

### **“I stumble”**

All participants mentioned that they literally and/or metaphorically stumbled. We identified four categories that illustrated their stumbling: pain and stiffness, fatigue, impaired balance and gait, and day-to-day fluctuations. Each category is addressed below and introduced with a representative quote.

*Sometimes the pain feels like I've been run over by a train (P2)*

Almost all participants consistently mentioned leg pain as an important factor in their life. Some also experienced back pain, which they thought was caused by an altered posture and gait pattern. Pain often had an impact on the patients' emotions. One person expressed that sometimes she felt she could not live with the pain anymore: *“I cannot explain it very well, but sometimes the pain is so unbearable that I would rather be dead” (P2).*

Another complaint mentioned by all participants was leg stiffness. Both stiffness and pain in the legs increased the longer a sitting or lying position had to be maintained. Initiating walking after a seated activity (e.g., playing the accordion) or walking to the coffee machine during a work break was inconvenient due to the stiffness. Also, participants experienced leg pain and stiffness during the night that led to difficulties with their mobility in bed: *“When I lie down, I am like a plank from my waist down. If I want to turn over, I have to move my legs with my hands and flip myself over”* (P3).

*I am so tired that I could sleep standing up* (P5)

Many participants expressed that living with spasticity was very taxing, leading to high levels of fatigue. They felt that, above all, their gait impairments required more effort and energy. Another presumed cause of fatigue was disturbed night-time rest due to difficulties in finding a comfortable sleeping position as well as with rolling over in bed. To be able to perform their basic and work-related activities as well as possible, they went to bed early and took naps during the day. Furthermore, physical activity levels were set lower so that energy could be preserved and then devoted meticulously to the most important daily activities, for instance during valuable leisure time: *“I do not enjoy walking, I only walk when it is really necessary. It exhausts me”* (P6).

*I have difficulty with all the activities that require me to use my legs* (P10)

All participants experienced problems with gait and balance control. They reported a gait pattern characterised by toe-walking and a diminished walking speed. They experienced a stumbling gait pattern and were afraid of falling or reported falls or near falls: *“When I walk downhill, I need to tilt my torso backwards quite a bit to avoid falling”* (P12). Due to both the impaired balance control and stumbling character of the gait, all standing and walking activities were considered by many as very energy demanding.

As a consequence, participants experienced limitations in a wide range of daily activities such as personal hygiene, housekeeping, gardening, employment, mobility including shopping and getting groceries, and leisure activities. They mentioned problems with standing still, regular walking, bending, and stepping across objects in addition to pain, stiffness, and fatigue as the factors underlying the limitations they experienced. They gave several examples to illustrate their problems in daily life. Participants explained that their personal hygiene was time-consuming and that it was difficult to complete the job in a standing position. Housekeeping was also problematic, in particular reaching for and cleaning low and high objects: *“I need to step over the cable and the hose when I’m using the vacuum cleaner, and I cannot do that”* (P3). Both housekeeping and gardening were fatiguing and demanded a lot of balance effort: *“I used to trim the hedge myself. I can still do the trimming, but I can’t manage to do the raking anymore. For that I need to be able to walk, and I can’t anymore”* (P1). Some participants reported that walking at work was difficult as

well, because they could not concentrate on their gait. For example, it was hard to stand up regularly to get a printed document or a cup of coffee.

Regarding outdoor mobility, the activities of getting in and out of a car and using the gas or brake pedals were also reported by many as problematic: *“I hope my driver’s license will be renewed since using the brakes is getting problematic”* (P8). Still, driving a car was very important to them to be able to visit people or go shopping. Only one participant did not have any problems driving a car. Riding a bicycle was also difficult because many participants were afraid of falling when using the brakes suddenly for stopping. Walking on an uneven surface, grit, or sand increased the risk of falling. Some people were accustomed to regular falls, but still feared that a fall one day might have serious physical consequences such as a bone fracture. Participants thought exercise and sports were important, but it was difficult to find a suitable sport given their physical limitations.

*Some days I feel like a wreck, but sometimes I don’t feel too bad at all* (P2)

Although some participants related that their symptoms and activity limitations were relatively stable over a certain period of days or weeks, others reported strong and often unpredictable fluctuations from day to day. As one participant said: *“When I walk to the car in the morning, I can feel whether it’s going to be a good or a bad day. I don’t know why that is, though”* (P9). Fatigue and physical stress were mentioned by some participants as a possible explanation for these fluctuations, but others had no explanation: *“Sometimes I walk 20 minutes through the village after work and have little discomfort, but I can’t manage to do that again the day after”* (P10). Besides day-to-day fluctuations, all participants experienced a gradual increase in disease progression, slowly leading to more activity limitations: *“In the past, I could step over a gate, nowadays I have to be careful at a doorstep”* (P2).

### **“I struggle”**

All participants used adaptation strategies to compensate for their physical limitations, which made life a struggle to many. They either continuously adjusted the performance of an activity to their actual limitations over the years, or they ultimately decided to quit the activity completely. Each of these two categories is elaborated below and introduced with a representative quote.

*I have to think before I do something: First I have to be standing steadily, then I can lift the groceries into the car* (P13)

Participants used a wide variety of aids and physical home adaptations. They also asked for support from their spouses or other close kin during more strenuous activities such as housekeeping and gardening. Participants sometimes found practical solutions for everyday problems, for example, bending was avoided by picking up a metal object with

a magnet or a shoe was picked up from the floor with a vacuum cleaner: *"I use a vacuum cleaner to pick something up from the ground. I put the nozzle in a shoe so that I can lift it"* (P7).

Participants regularly used walking aids such as a cane, walker, orthopaedic shoes, or ankle-foot orthoses. Additionally, they used a trolley to walk better, safer, and to disguise their gait and balance difficulties: *"I can walk well with a shopping trolley and no one notices I have a problem; I can imagine that I will need a walker later. But as long as I don't need to, I don't use one yet"* (P11). For transportation across long distances, participants preferred cycling to walking and many used a power-assisted bike rather than a regular bike to save energy. Some, however, preferred riding a regular bike as long as possible to optimise and maintain their physical endurance level.

Another adaptation strategy was to increase the level of conscious attention to perform certain activities. Participants walked with increased visual control by watching the floor to be able to anticipate and avoid obstacles. Some explored unfamiliar target areas during the day or at quiet moments in anticipation of night-time activities or crowded places: *"During the day I check the surroundings so that I will know where the obstacles are when it is dark, or when it is very busy"* (P7). While riding a bicycle, they searched for a quiet place to slow down and safely dismount from their bike. They planned their shopping route in advance to reduce the walking distance and to save as much energy as possible. Lifting heavy groceries into the car demanded preparation for stable standing to prevent falling.

Even though most adaptation strategies required increased attention and mental awareness, participants felt that, on the one hand, these strategies enabled them to keep performing important activities, which gave them a feeling of independence. On the other hand, all participants expressed that applying adaptation strategies had a huge impact on their daily lives: *"I would love to not have to think about it when I go somewhere. For instance, what will we be doing on a staff outing? Will I be able to keep up, and will I be able to sit down somewhere along the way to rest? Can I park near my destination or do I still need to walk a certain distance?"* (P4). In addition, finding the right balance between being active and taking rest was considered very difficult. While insufficient movement increased stiffness and hampered gait, too much physical activity resulted in reduced leg stability and loss of balance.

*Diving is now impossible because I can't control my feet any more* (P8)

Participants indicated that, at a certain point in time, applying adaptation strategies to keep up physical activities was no longer possible. For example, they quit regular group exercises once it became too hard for them to follow the pace of the group: *"I gave up Nordic Walking because I could no longer keep up with the group. They always had to wait for me. I'm having to give up more and more things these days. That's a real shame"* (P11).

When patients were unable to perform certain activities due to a lack of motor skills, they sometimes searched for other, less demanding activities to be able to fulfil a specific social role. For instance, one participant started volunteering in a nursing home to hand out coffee and tea instead of teaching swimming skills to disabled people. Another started to do maintenance activities at his tennis club instead of being an active tennis player.

Quitting activities also affected professional employment. For many participants, doing their job was too exhausting or the required activities had become physically impossible. They found that sound lower-limb function, an appropriate sitting posture, and sufficient energy level was needed for almost every job, which often made finding an alternative position more difficult.

### **“I feel ashamed”**

Many participants expressed feelings and thoughts about themselves and reflected on how others might think about them. Feeling judged and ashamed was a very significant category of emotions. Another category of emotions was feelings of fear and frustration. Each of these two categories is elaborated below and introduced with a representative quote.

*At parties I don't drink much wine, otherwise they think I'm drunk (P11)*

Participants regularly encountered negative judgements by persons in their social environment, or felt ashamed of how they walked because of looks or comments from others: “People look at me, they think I'm crazy because I walk so strangely” (P8). The feeling of being observed worsened their gait pattern even more: “When I was on holiday in Rome, I felt much more relaxed walking through the city because nobody knows me there” (P11). Several participants also had to endure other people's opinions, particularly concerning questions about the need for walking aids or mobility devices: “Everyone asks, ‘aren't you too young to be using an electric scooter?’” (P2). Among friends, participants could talk freely about spasticity and its consequences in daily life, although they showed less openness amongst others.

*I am so scared that I will deteriorate further (P13)*

Living with chronic spasticity led to feelings of fear, frustration and depression. Participants feared the slow but inevitable progression of their disease. They tried to stay as active as possible to prevent functional decline. Some avoided the use of walking aids, such as ankle-foot orthoses, because of fears that using such aids might make their muscles even weaker and lead to a more rapid functional decline. Participants experienced feelings of frustration since their social roles gradually became more restricted. Being more homebound also led to having fewer topics to discuss with other people. Some participants found it very difficult to accept the consequences of spasticity, or became

angry with themselves when, for example, they could not get out of bed easily. Some even felt depressed, wondering why they were affected by chronic and progressive spasticity.

### **“I need support”**

All participants needed some type of support for dealing with chronic spasticity and its functional consequences. The question on their needs and expectations regarding spasticity management elicited explicit ideas about how participants wanted to be supported by professional healthcare providers. We identified four categories: adequacy of information, efficacy of interventions, quality of healthcare professionals, and insight into disease progression and day-to-day fluctuations. Each category is addressed below and introduced with a representative quote.

*I want more information than just the explanation about what the abbreviation HSP means (P5)*

Both participants and caregivers mentioned the need of appropriate information about spasticity and its individual consequences: *“My partner and I both suffer from the effects of spasticity. We both want to learn more about this”* (P5). Participants not only expressed their need of adequate medical information, but also of practical information about how to deal with the consequences of spasticity in daily life. The need for appropriate information was underlined by one patient who stated that she did not want botulinum toxin injections yet, because she was afraid that the effectiveness might wear off over time. Then, when she would really need the injections, they might no longer be effective. Furthermore, she brought up the issue of high costs and the relatively short duration of effects, from which she concluded it would be best to postpone the injections: *“Maybe I’ll get more out of those injections when I get older. Is it still too soon? ..... And even though I don’t have to pay for them myself, the prices are shocking”* (P13).

*Thanks to the injections, the tips of my shoes don’t need to be repaired so often (P7)*

Regarding the efficacy of interventions, beneficial experiences with botulinum toxin injection were mentioned. Participants experienced a slower progression of spasticity-related problems. A negative effect mentioned by several participants was the initial weakness in their legs after the injections, leading to a wobbling gait and loss of stance stability: *“The first few days, my legs are weaker, making me wobblier. I have less control over my legs then”* (P10). Participants experienced the benefits of the injections only after the first few days. The effect of botulinum toxin wore off after a time. Participants told that the resulting increase in spasticity-related problems was unpleasant and that they wanted to avoid this. Therefore, some participants preferred a fixed schedule of injections, as they were afraid of receiving their follow-up treatment too late. Some participants did not receive any injections, but were treated with oral spasmolytics. These patients experienced

fatigue, sometimes extreme, which they felt was a side effect of the medication. Someone explained that she fell asleep while having visitors, and this was mentioned as a burden.

Many participants performed stretching exercises, either by themselves or supported by a physiotherapist, or a combination of both. Some participants mentioned that they had to stretch their leg muscles daily, since physiotherapy twice a week was not sufficient to reduce their discomfort. Some participants preferred to incorporate stretching exercises into their daily routines: *"I stretch my calves at the kitchen worktop while I make my sandwiches for breakfast. That way I won't forget to do those exercises"* (P4). Others, however, found that physiotherapists were able to stretch their muscles more effectively than they were able to do themselves. Many considered a combination of physiotherapy and a home-based exercise program to be an optimal solution, as they needed coaching and motivational support to perform the home exercises. Only a few participants did not experience a beneficial influence of physiotherapy in addition to self-treatment. Some experienced no difference when they interrupted their (self-)treatment during the holiday season.

*My GP ... does not know much about this (P1)*

Participants were usually satisfied about the healthcare providers in centres of expertise for HSP, because their treatment was based on a thorough and personalised assessment. Participants felt they were taken seriously, were able to contact the professionals easily, and experienced a relationship of trust as most of the professionals reacted promptly and adequately to their questions and needs. In contrast, they were less satisfied with the healthcare providers in the community, both general practitioners and physiotherapists. They felt that most of these professionals were unfamiliar with HSP. They also commented on the absence of a thorough assessment, personalised instruction and treatment, easy access, regular check-ups, and shared decision-making. Although treatment close to their homes was convenient, some participants experienced discontinuity or felt that therapists went too easy on them during therapy: *"I would really like to receive proper treatment, and not just do the same exercises that I already do at home"* (P2).

*The symptoms creep up on me, but with a video I could see the difference (P8)*

Although participants did not want to be confronted too much with the progression of their disease, they did want to get better grip on their condition by receiving feedback about spasticity fluctuations and the influence of interventions on their possibly fluctuating spasticity. They explained that it would be easier to adhere to the exercise plan if they could notice the effects of their efforts. Furthermore, they thought that objective feedback would provide insight into whether an experienced change was real or not. Monitoring their functional status regarding the joint range of motion, muscle length, gait velocity, gait pattern, pattern of rising and sitting down, and sleep patterns were mentioned as important: *"I would like to keep track of the of quality of movement, and*



*make connections between the walking speed, stiffness, and the length of my calf muscles"* (P6). Participants felt that the use of wearable devices or short video assessments could be helpful in this respect, yet that monitoring should be undemanding and not be time-consuming. Some participants took their own initiative to monitor their experiences after change of medication: *"When I switched from baclofen to botulinum toxin, I made a note of the changes I noticed in my phone"* (P4).

## Discussion

This qualitative study investigated the experiences and needs of patients with chronic spasticity due to a pure form of HSP at the level of physical activities, social participation, and general well-being. Based on semi-structured interviews with 14 purposively selected patients, four common themes were identified that are reflected by the following phrases: (1) "I stumble", (2) "I struggle", (3) "I feel ashamed", and (4) "I need support". Participants literally or metaphorically stumbled when performing a wide range of physical activities. Applying adequate strategies to manage spasticity and its consequences was often perceived as a struggle in terms of the medical, role, and emotional management [16]). Furthermore, participants often felt ashamed as they experienced negative judgements by persons in their environment. Finally, they expressed the need for medical and practical support not only from professionals working in centres of expertise, but also from community healthcare professionals. In table 2, we have summarised some of the important messages from the participants.

**Table 2:** Key messages from the participants

Theme	Category	Important message
I stumble	Pain and stiffness	Pain and stiffness are cardinal features of HSP.
	Fatigue	Fatigue is a major consequence of spasticity, impacting on both daily routines and night rest.
	Impaired balance and gait	Limitations in gait and balance have an impact on almost all physical activities.
	Day-to-day fluctuations	Within the gradual progression of spasticity, participants experience substantial day-to-day fluctuations.
I struggle	Adjustment to limitations	Spasticity is energy demanding.
	Quitting activities	Giving up activities is common in various domains of daily life. Finding alternatives is a struggle.
I feel ashamed	Feeling ashamed and being judged	Moving differently than others causes feelings of shame and being judged.
	Feelings of fear and frustration	Fear of functional deterioration and frustration about gradually increasing social isolation are common.
I need support	Adequacy of information	There is a need for reliable medical information as well as practical information on how to deal with spasticity.
	Efficacy of interventions	Botulinum toxin injections induce fluctuations of spasticity, which are inconvenient. Physiotherapy can provide coaching and motivation to continue home exercises over time.
	Quality of healthcare professionals	Healthcare providers in expertise centres should support healthcare providers in the community with specific knowledge of how to treat and coach patients with HSP.
	Insight in progression and fluctuations	Monitoring of physical impairments and activity limitations is important to get a better grip on the consequences of lower-limb spasticity on daily life.

### **Spasticity is more than just stiffness**

Participants reported some well-known physical consequences of chronic lower-limb spasticity, such as stiffness, leg pain, and a stumbling gait pattern [9, 17]. In addition, they mentioned less obvious consequences of lower-limb spasticity, such as back pain, fatigue, and unpredictable day-to-day fluctuations. Besides leg pain, nearly all participants complained about lower back pain, which they believed to be due to an altered posture and gait pattern. They also experienced that both a strenuous gait and a disturbed sleeping pattern were responsible for high levels of fatigue. Together, these symptoms had a huge impact on their daily lives. Notably, pain and fatigue have been scarcely addressed in the literature on HSP, even though they are regarded by the patients as some of their most disabling symptoms [18]. This observation underscores the importance of monitoring fatigue and pain levels in persons with chronic spasticity, and of integrating energy and pain management strategies into the rehabilitation regimens for people with HSP.

### **The need to address outcomes that are meaningful to the patient**

Cusick et al (2015) argued that the most frequently used measurement tools in the rehabilitation of chronic spasticity are focused on the level of physical impairments, particularly measures of muscle tone and joint range of joint motion [7]. Although these are relevant outcome measures from a medical perspective, they do not address the issues that are most relevant to the patients, such as fatigue, pain, sleep, and general well-being. Outcomes that address fatigue, energy expenditure, and sleep appear to be lacking in the literature on chronic spasticity in persons with HSP. Incorporating such measures into the treatment regimens for chronic spasticity may help to tailor interventions to the needs of individual patients.

In addition to physical impairments, all participants experienced serious limitations across a wide range of physical activities, including the domains of personal care, domestic life, employment, and leisure. Apart from the publication by Grose et al. [17], who found similar limitations, the literature on HSP has scarcely addressed the extent to which chronic spasticity impacts on these physical activities, and how patients contend with their physical activity limitations and related participation restrictions. According to the new definition of health by Huber et al (2011), health is not the absence of disease, but the ability to adapt to the consequences of disease and being able to self-manage these consequences [19]. This definition implies that healthcare providers should not only assess physical impairments and the manner in which these are managed by patients (medical management), but should also systematically evaluate the performance of daily activities and the level of participation to understand the impact of spasticity on the daily life of the individual patient with HSP (role and emotional management).

Against the above-mentioned background, measuring relevant outcomes identified by persons with chronic spasticity, referred to as patient-reported outcomes (PROs), can be helpful to tailor interventions to individual needs [20] and to develop personalised monitoring strategies throughout the course of the disease. At present, patient-reported outcome measures (PROMs) that have been developed for and used by people with chronic hereditary spasticity are lacking, although the Spastic Paraplegia Rating Scale (SPRS), validated for patients with hereditary spastic paraplegia [21], may be a valuable alternative tool. This study has identified several functional aspects, such as spasticity-related fatigue, pain, sleeping problems, and activity limitations, for which PROMs must be developed.

### **Personal feedback enhances individual grip on spasticity**

Participants explained that they had difficulties gaining control of the changes in their spasticity levels, either changes that occur spontaneously or those induced by interventions. For instance, participants found it difficult to differentiate between disease progression and the wearing-off phenomenon following focal spasmolysis. In addition, participants reported that both internal factors (stress, fatigue) and external factors (temperature) could influence spasticity. To enhance the patients' control over spasticity, they expressed the need to have insight into the relevant changes that occur over time. Systematic monitoring of PROs may help both patients and professionals to monitor disease progression and to evaluate the effect of interventions [20]. In addition, professionals should meticulously monitor the status of several bodily functions and capacities, because slight but gradual changes in, for example, muscle length may eventually have a negative impact on the performance of activities.

The monitoring of PROs would seem to be a mutual responsibility between the professionals and patients. Indeed, the benefits of self-monitoring have already been demonstrated: patients with chronic obstructive pulmonary disease and in patients with cerebral palsy were able to detect relevant changes in their health condition [22], which reduced long-term complications [23].

### **Empowering patients' capacity for adaptation and self-management**

Our participants reported a difference between healthcare professionals in expertise centres and those in community-based centres. Particularly, they missed sufficient expertise when they consulted their general practitioner and/or physiotherapist in the community. They felt that treatment quality could be enhanced by more knowledge of the consequences of spasticity in everyday life. In addition, they needed more personalised instruction and coaching on how to adapt to these consequences (role and emotional management). Therefore, it seems important that healthcare providers in expertise

centres exchange their knowledge with healthcare providers in the community to avoid a mismatch regarding goals and priorities for rehabilitation.

Such mismatches have been reported for the stroke population [24] and for persons with Parkinson's disease [25]. For example, in a systematic review, Jellema et al [26] showed that public belief and support from others were crucial for patients with stroke to overcome their barriers to perform certain activities. In addition to the education of stroke patients regarding home, work, and community activities and possible adaptation strategies, they recommended providing stroke survivor's proxies with the knowledge and skills to encourage patients to resume their social participation [26]. From this perspective, patients with HSP and their close kin should also be taught adaptation strategies to reduce the consequences of chronic spasticity in their daily lives. To achieve this aim, an interdisciplinary approach may be necessary including contributions from occupational therapists and psychosocial disciplines.

### **Strengths and limitations**

This study has a number of strengths. We used the COREQ criteria for reporting qualitative research [14]. The data were collected by means of interviews at the participants' homes, which created a comfortable and safe atmosphere. A member check was performed by presenting the conversational notes to the participants and allowing them to check the accuracy. The procedure for data collection and analysis as well as the results were reviewed together with the second author, and eventually with the entire research team. A limitation of this study is that intimate topics, such as bladder issues or sexuality, although mentioned in the literature [9], were not addressed by our participants. Reasons for not mentioning these topics by our participants might be feelings of shame and the possibility that they associated spasticity primarily with impairments of the lower limbs rather than with bladder or sexual dysfunction. Another limitation is that the results remain limited to patients with a pure form of HSP, and do not include the more complicated subtypes. As a consequence, the results cannot be generalised to other HSP populations.

### **Conclusion**

This study shows that the consequences of chronic lower-limb spasticity in patients with pure forms of HSP go beyond the well-known consequences such as muscle stiffness and impaired ambulation. HSP is associated with fatigue, pain, unpredictable day-to-day fluctuations, a wide range of physical activity limitations and social participation restrictions, and the continuous need to adjust compensation strategies to overcome these limitations. In addition, feelings of shame, fear, frustration, and depressed mood coincide with the disabilities experienced and the judgements made by persons in the social environment. The participants expressed a strong need for interventions not only to reduce the neuromuscular impairments, but also to alleviate fatigue and pain, to improve

night-time rest, and to restore the capacity to perform relevant physical activities and fulfil social roles. Spasticity rehabilitation regimens should therefore be tailored to the individual needs of the person with HSP, based on careful personalised monitoring that includes patient-reported outcomes. Enhancing self-management may empower patients to gain control of the consequences of chronic spasticity in their daily lives.

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### **Competing interests**

The authors report no conflicts of interests.

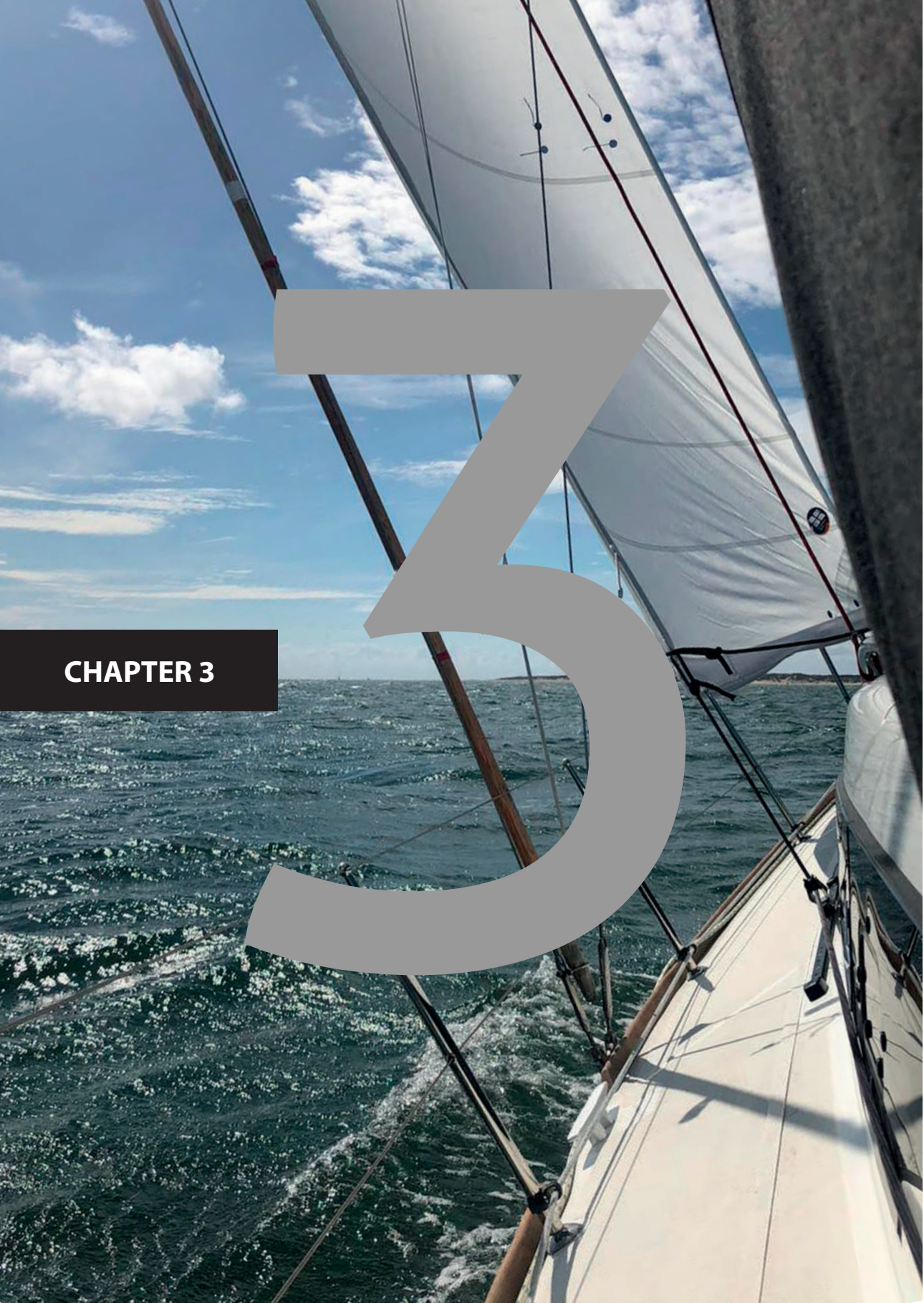
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**CHAPTER 3**

# Experienced complaints, activity limitations, and loss of motor capacities in patients with pure HSP

van Lith BJH, Kerstens HCJW, van den Bemd LAC, der Sanden MWGN, Weerdesteyn V, Smeets RJEM, Fheodoroff K, van de Warrenburg BPC, Geurts ACH. Experienced complaints, activity limitations and loss of motor capacities in patients with pure hereditary spastic paraplegia: a web-based survey in the Netherlands. *Orphanet J Rare Dis.* 2020 Mar 4;15(1):64. doi: 10.1186/s13023-020-1338-4



## **Experienced complaints, activity limitations and loss of motor capacities in patients with pure Hereditary Spastic Paraplegia: a web-based survey in the Netherlands**

### ***Background***

Hereditary spastic paraplegia (HSP) is a group of inherited disorders characterized by progressive lower limb spasticity. Treatment is often focused on reducing spasticity and its physical consequences. To better address individual patients' needs, we investigated the experienced complaints, activity limitations, and loss of motor capacities in pure HSP. In addition, we aimed to identify patient characteristics that are associated with increased fall risk and/or reduced walking capacity.

### ***Methods***

We developed and distributed an HSP-specific online questionnaire in the Netherlands. A total of 109 out of 166 questionnaires returned by participants with pure HSP were analyzed.

### ***Results***

Participants experienced the greatest burden from muscle stiffness and with standing and walking activities, while 72% reported leg and/or back pain. Thirty-five and 46% reported to use walking aids (e.g. crutches) indoors and outdoors, respectively; 57% reported a fall incidence of at least twice a year ('fallers'); in 51% a fall had led to an injury at least once; and 73% reported fear of falling. Duration of spasticity and incapacity to rise from the floor were positively associated with being a 'faller', whereas non-neurological comorbidity and wheelchair use were negatively associated. Higher age, experienced gait problems, not being able to stand for 10 minutes, and incapacity to open a heavy door showed a negative association with being a 'walker without aids' (>500m).

### ***Conclusions***

Our results emphasize the large impact of spasticity on the lives of people with pure HSP and contribute to a better understanding of possible targets for rehabilitation.

Keywords: Hereditary spastic paraplegia; spasticity; survey; falls; gait; rehabilitation

## Background

Hereditary spastic paraplegia (HSP) is a group of inherited disorders, characterized by progressive bilateral lower limb spasticity (LLS) and, to a lesser extent, muscle weakness [1]. HSP can be classified as 'pure' ('uncomplicated') or 'complicated', depending on the presence of other neurologic abnormalities such as ataxia, seizures, cognitive impairment, and/or involvement of the upper extremities and speech [2,3,4,5]. In patients with pure HSP, the main neurological feature is progressive LLS. As spasticity cannot be cured, treatment is often focused on reducing or stabilizing spasticity and its physical consequences. However, rehabilitation strategies should also specifically focus on (other) experienced complaints and activity limitations in order to address the needs of patients. Thus, gaining more knowledge of LLS-related complaints, activity limitations, and loss of motor capacities as experienced by patients is important for better disease management and tailoring interventions to individual patients' needs.

In various patient groups with LLS (e.g. stroke and multiple sclerosis), spasticity appears to be a significant contributor to experienced complaints, activity limitations, and loss of motor capacities [6,7,8]. Recently, a general international survey in patients living with spasticity was conducted that emphasized the large impact of spasticity on daily life and the need for better collaboration, communication and sharing of information between patients and their healthcare providers to fulfill individual needs [9]. Yet, patients with pure HSP may differ from the population with LLS at large, as their condition is inherited and slowly progressive. Existing reports on pure HSP typically indicate the presence of gait and balance impairments and an increased risk of falling as the most prominent functional consequences of HSP [5,10,11,12,13,14]. In addition, some studies mentioned the occurrence of pain, fatigue, urinary symptoms, sleeping problems, unpredictable day-to-day fluctuations, activity limitations and participation restrictions. However, these studies included either small patients samples [15,16] or lumped patients with pure and complex HSP [17,18,19].

Against this background, we developed a disease-specific online questionnaire to investigate the experienced complaints, activity limitations, and loss of motor capacities as well as the experienced healthcare needs in a large, representative group of patients with pure HSP in the Netherlands. In the current study, we specifically focus on LLS-related complaints, activity limitations and loss of motor capacities to better understand the impact of the disease. In addition, as balance and gait impairments are considered key problems in HSP, we aimed to identify specific demographic, clinical and functional characteristics that are associated with increased fall risk and/or reduced walking capacity. Data on the experienced needs will be reported in a separate publication.

## Methods

### Recruitment and inclusion of participants

Participants were recruited through the national patient organization for neuromuscular disorders in the Netherlands (“Spierziekten Nederland”; [www.spierziekten.nl](http://www.spierziekten.nl)). On our request, they sent all the members of the HSP working group an e-mail with information about the web-based survey. In addition, all patients with pure HSP known at the national expertise center for inherited movement disorders of the Radboud university medical center in Nijmegen were sent a letter with information about the survey. Persons with HSP and their relatives were requested to contact primary researcher (BvL) by e-mail if they were willing to participate. After receiving an e-mail, the primary researcher sent a unique link to the web-based questionnaire to each patient who had indicated willingness to participate. This study was approved by the regional medical ethics committee “Commissie Mensgebonden Onderzoek Arnhem-Nijmegen” (number 2016-2922) and conducted according to the declaration of Helsinki.

### Web-based questionnaire

The structure and content of the web-based survey were designed by a team of expert physicians, researchers, physical therapists, and persons with HSP. Part of the questionnaire was based on a previous international survey of patients living with spasticity [9], while other questions were based on a qualitative study in patients with pure HSP who were interviewed about the consequences of spasticity on their daily lives and their related healthcare needs (note: data on healthcare needs are reported elsewhere) [16]. Completion of the questionnaire by participants was estimated to take about 20 minutes, but there was no set time limit. Participants were able to pause the questionnaire and continue later. To some extent, the amount of questions was variable for each participant, depending on his/her answer to a preceding question. Answering options were based on multiple choice, but some questions included a text entry as one of the options. Overall, the questions in this study were grouped into three response categories: A. ‘participant characteristics’, B. ‘complaints and activity limitations’, and C. ‘loss of motor capacities’. Whereas the questions in category B were focused on the problems participants experienced when performing certain daily life activities, the questions in category C were focused on the self-rated capacity to execute specific activities.

### Data analysis

To obtain a homogeneous sample of persons with symptomatic pure HSP, the questionnaire included specific questions to identify patients with neurological comorbidity and/or a complicated form of HSP. Patients were excluded from further analysis if they indicated that they had a complicated form of HSP (or a genetic defect invariably associated with a complicated form of HSP); experienced upper limb paresis, speech problems, or cognitive

problems; or reported any neurological comorbidity that could influence spasticity, motor control, physical fitness, or activity. As we were interested in LLS-related complaints, activity limitations, and loss of motor capacities, participants who reported that they did not experience spasticity (or had spasticity for less than 1 year) were also excluded from further analysis.

### **Statistical analysis**

Descriptive statistics were used to analyze the primary data obtained from the questionnaires. In addition, univariate logistic regression analyses were performed on two dependent variables: being a 'walker without aids' (i.e., self-report of walking distance without crutch or walker > 500m), and being a 'faller' (i.e., self-report of at least two falls a year). To prevent overfitting of the model in case of many correlations between possible determinants and dependent variables, we continued with multivariate logistic *forward* regression analyses. Thus, possible determinants from each of the four response categories that were associated with a specific dependent variable in the univariate analyses ( $p < 0.10$ ) were entered in a multivariate logistic forward regression analysis ( $p < 0.05$ ) to identify clinically relevant, independent determinants for this dependent variable.

## **Results**

### **A. Participant characteristics**

A total of 194 respondents requested to participate, of which 166 persons returned a fully completed questionnaire. Subsequently, 57 respondents not meeting the criteria outlined above were excluded ( $n=16$  complicated HSP;  $n=12$  upper limb paresis;  $n=21$  speech problems;  $n=19$  cognitive problems;  $n=15$  neurological comorbidities;  $n=4$  spasticity < 1 year). Finally, 109 respondents were included for further analysis. The participants showed an equal sex distribution (49.5% male and 50.5% female) and had a mean age of 52.8 years (age range 19-84 years). Most participants (83%) indicated a positive family history for pure HSP and 53% reported that HSP was also genetically confirmed. Participants without a positive family history or genetic diagnosis ( $n=7$ ) were e-mailed by the primary investigator to confirm that the clinical diagnosis of pure HSP was made by a neurologist. All participant characteristics are summarized in table 1.

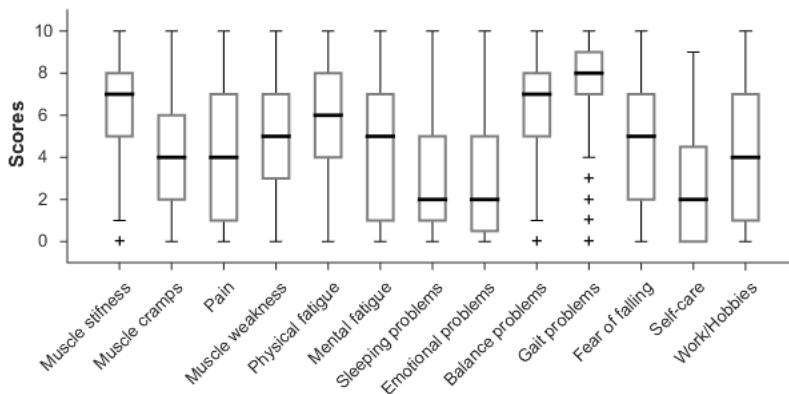


**Table 1:** Demographic and clinical characteristics (N=109)

<b>Patient characteristics</b>	<b>n</b>	<b>mean (SD)</b>
Sex (male/female)	54/55	
Age (years)		52.8 (14.2)
<b>Duration LLS symptoms (years)</b>		
1-5 years	21	
6-10 years	21	
11-15 years	16	
> 15 years	51	
<b>Genetic defect</b>		
SPG-3a	4	
SPG-4	36	
SPG-5a	2	
SPG-7	3	
SPG-8	3	
SPG-10	2	
SPG-17	1	
SPG-31	5	
SPG-72	1	
<b>Positive family history</b>		
First degree relatives	83	
Other family members	47	
First degree relatives and/or other family members	90	
Unknown	10	
No	14	
<b>Non-neurological comorbidities</b>		
Asthma/COPD	6	
Diabetes	1	
Hypertension	9	
Joint disorders	13	
Cardiac problems	4	
Other non-neurological comorbidities	7	

## B. Complaints and activity limitations

Experienced complaints and activity limitations were scored on a numeric scale (range 0-10; 0: no burden/hindrance, 10: extreme burden/hindrance). Overall, the participants experienced the greatest burden or hindrance from their muscle stiffness and with performing standing and walking activities (figure 1). Sleeping problems, self-care problems, and emotional problems were relatively mild.



**Figure 1:** Median, interquartile range, and total range of the level of burden/hindrance that participants experienced in various categories (Questions B1-B13) (0: no burden/hindrance, 10: extreme burden/hindrance). +: outlier.

Seventy-two percent of the participants reported chronic pain. Fifty-five participants (50%) reported back pain, predominantly in the lower back, and 59 participants (54%) reported leg pain. The majority described leg pain as nerve pain ( $n=25$ ), cramps ( $n=32$ ), or restless legs ( $n=33$ ).

### **Autonomic dysfunctions**

Forty-nine (50%) and 21 (19%) of the participants reported micturation and defecation problems, respectively. These problems were related to extreme urge ( $n=22$  and  $n=11$ , respectively), sphincter control ( $n=45$  and  $n=14$ , respectively), or slowness of gait ( $n=30$  and  $n=11$ , respectively). Forty-three of the participants (39%) reported sexual problems, whereas 46 (42%) experienced no sexual problems and 20 did not know (18%). The most frequently reported reasons for sexual problems were related to spasticity ( $n=26$ ) and pain ( $n=14$ ). Some men reported ejaculation problems ( $n=4$ ) or erectile dysfunction ( $n=8$ ), whereas some women experienced vaginal dryness ( $n=5$ ). Eleven participants reported other sexual problems, among which difficulties with having an orgasm ( $n=6$ ).

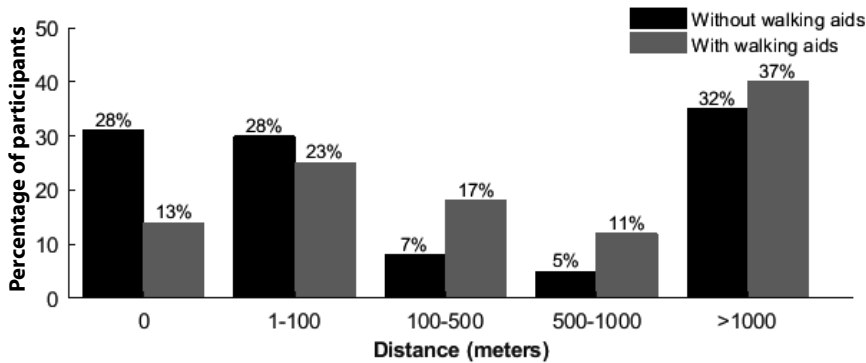
### C. Loss of motor capacities

Table 2 provides an overview of the devices applied for supporting functional mobility. The devices were categorized into orthoses (including orthopedic footwear), walking aids, and wheelchairs. The most often used devices were walking aids, such as canes or crutches: 35% reported to use walking aids indoors, whereas 46% used walking aids outdoors. Outdoors, an (electric) wheelchair was often applied as an alternative for walking.

**Table 2:** Use of mobility-supporting devices (N=109)

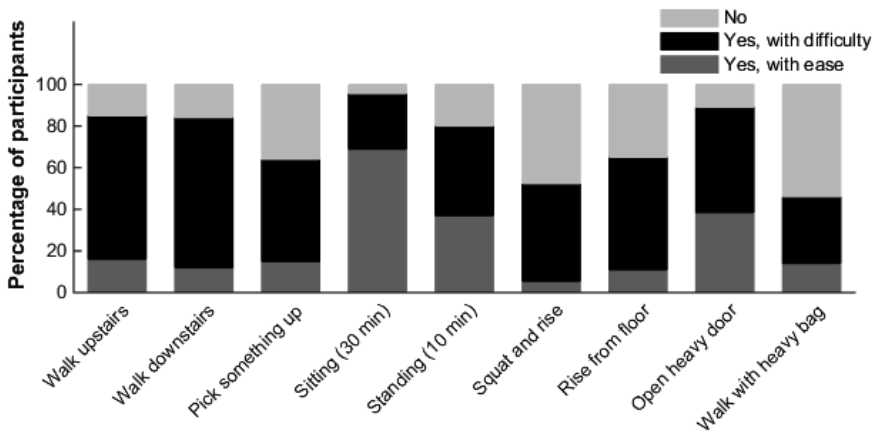
Type of device	n (%)	
	Indoors	Outdoors
Orthoses	32 (29%)	44 (40%)
<i>Ankle-foot orthosis</i>	13 (12%)	19 (17%)
<i>Orthopedic footwear</i>	28 (26%)	34 (31%)
Walking aids	38 (35%)	50 (46%)
<i>Walker</i>	26 (24%)	30 (28%)
<i>Cane/Crutch</i>	28 (26%)	41 (38%)
Wheelchairs	23 (21%)	50 (46%)
<i>Wheelchair</i>	22 (20%)	43 (39%)
<i>Electric wheelchair</i>	7 (6%)	29 (27%)
Other	11 (10%)	10 (9%)
None	44 (40%)	23 (21%)

Without walking aids, the majority of the participants was able to walk either 0 to 100 meters (56%) or more than 1000 meters (32%). Only 37% was able to walk at least 500 meters without a walking aid. With the use of walking aids, there was a more equal distribution of walking capacity due to a general shift from very short to longer distances (figure 2). Indeed, a total of 45 participants (41%) was able to walk further with than without the use of a walking aid. Many participants described their gait pattern as characterized by drop foot (75%), scissoring (30%), and/or crouch gait (13%).



**Figure 2:** Walking distance with and without aids.

As shown in figure 3, relatively few participants were not able to sit for 30 minutes or to open a (heavy) door. In contrast, stair walking, picking something up from the floor, squatting and rising, rising from the floor, and walking with a heavy bag was difficult or even impossible for the majority of the participants.

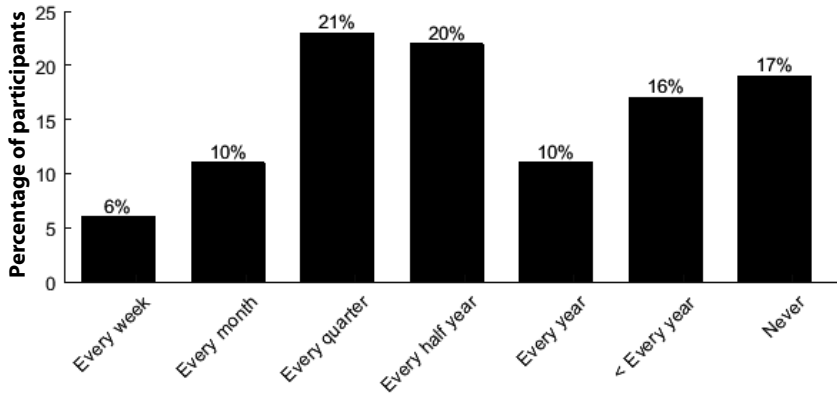


**Figure 3:** Percentage of participants that responded to be able to execute specific motor capacities with ease, with difficulty or not at all.

**Falls**

Since the onset of LLS symptoms, 93 of the participants (85%) had fallen at least once, which had occurred within 5 years of symptom onset in 63 of 93 subjects (68%). Most participants (67%) reported a fall incidence of at least once a year; 57% reported to fall at least twice a year ('faller') (figure 4). In 56 participants (51%) a fall had led to an injury at

least once, such as a skin injury (n=34), bruise (n=33) and/or bone fracture (n=13). Only 29 of the participants (27%) reported not to be afraid of falling, whereas 66 (60%) were moderately afraid and 14 (13%) were very afraid to fall!



**Figure 4:** Self-reported fall frequency of participants.

### Regression analyses

Univariate logistic regression analyses (n=109) revealed nine determinants that were associated with being a ‘faller’. These determinants were entered into a multivariate forward regression analysis (table 3, upper part). In the final model, duration of LLS symptoms and the incapacity to rise from the floor were positively associated with being a faller, whereas non-neurological comorbidities and the use of a wheelchair were negatively associated. The overall explained variance was 45%.

The 27 participants who were not able to stand for 10 minutes or who were not able to open a heavy door, were never able to walk more than 500 meters without walking aids. These participants could not be included in the (multivariate) logistic regression, because of the 1:1 associations. Univariate logistic regression analyses of the remaining participants (n=82) yielded 29 determinants that were associated with being a ‘walker without aids’. These determinants were entered into a multivariate forward logistic regression analysis (table 3, lower part). In the final model, difficulties with standing for 10 minutes and with opening a heavy door showed a strong negative association with being a ‘walker without aids’, whereas age and experienced gait problems showed a small to moderate negative association, respectively. The overall explained variance was 58%.

**Table 3:** Multivariate forward logistic regression analyses

Dependent variable: 'faller' (self-report of at least two falls a year) (n=109)				
Cofactor	Level of cofactor	n	OR (95 % CI)	p-value
<b>Duration of LLS symptoms</b>	<i>Reference:</i> 1-5 years	21		
	5-10 years	21	39.070 (5.405-282.410)	<0.001
	10-15 years	16	7.789 (1.419-42.757)	0.018
	>15 years	51	18.025 (3.813-85.220)	<0.001
<b>Comorbidity</b>	<i>Reference:</i> No	101		
	Yes	8	0.162 (0.052-0.509)	0.002
<b>Walking aids indoors</b>	<i>Reference:</i> No wheelchair	87		
	Wheelchair	22	0.130 (0.029-0.577)	0.007
<b>Rise from floor</b>	<i>Reference:</i> Yes, with ease	12		
	Yes, with difficulty	59	17.897 (2.759-116.108)	0.002
	No	38	17.934 (2.333 -137.878)	0.006
Overall explained variance R <sup>2</sup> = 0.450				
Dependent variable: 'walker without aids' (self-report of walking distance without crutch or walker > 500 m) (n=82)				
Cofactor	Level of cofactor	n	OR (95 % CI)	p-value
<b>Age</b>	19-84	82	0.944 (0.899-0.994)	0.030
<b>Gait problems</b>	0-10	82	0.604 (0.400-0.911)	0.016
<b>Standing (10 min)</b>	<i>Reference:</i> Yes, with ease	40		
	Yes, with difficulty	42	0.286 (0.085-0.970)	0.045
<b>Open heavy door</b>	<i>Reference:</i> Yes, with ease	41		
	Yes, with difficulty	41	0.165 (0.049-0.564)	0.004
Overall explained variance R <sup>2</sup> = 0.583				

## Discussion

Given the estimated prevalence of 800 persons with pure HSP in the Netherlands [20], this web-based survey probably included a fairly representative sample of 109 persons who showed an equal sex distribution, a wide age range, a large variation in LLS symptom duration, and an expected (skewed) distribution of underlying genetic defects. This study sample reported many subjective complaints and activity limitations, of which muscle stiffness and problems with performing standing and walking activities were most severe (medians  $\geq 7$  on a numeric rating scale 0-10). Muscle cramps, weakness, and (physical and mental) fatigue were also prominent, as were fear of falling and problems with performing working and hobby activities (medians 4-6). Remarkably, 50% of our sample

reported (low) back pain and 54% leg pain of variable character. In addition, 50% reported micturation problems, 19% defecation problems, and 39% sexual problems. In terms of gait capacity, 35% used walking aids indoors, and 46% outdoors. Walking aids particularly had an impact on persons with low ambulatory capacity, who were able to improve their walking distance from 0-100 meters to 100-1000 meters with aids. No more than 37% of the participants were able to walk 500 meters without aids. With regard to other gross motor capacities, the majority experienced problems with stair walking (upstairs and downstairs), picking something up from the floor, squatting and rising, rising from the floor, and walking while carrying a heavy bag. On top of that, the majority (57%) reported a fall incidence of at least twice a year.

### **Balance, gait and falls**

Several studies have reported problems with performing standing and walking activities and an increased fall risk in patients with HSP [4,11,12,13,14], but the published data on severity or prevalence of these problems are still very limited. Only one survey reported that 47% of the participants with HSP had fallen at least once over the past three months [18], yet this estimate also included patients with complicated forms of HSP. In the current survey, both the reported severity of the balance and gait problems, fear of falling, and the high prevalence of falls and fall-related injuries indicate that safe and efficient postural and ambulatory control is a major problem in people with pure HSP. The reported fall incidence of 67% for at least one fall per year seems to be relatively high compared to the majority of other patients with LLS (caused by e.g. multiple sclerosis, stroke or cerebral palsy) of whom 50-68% report at least one fall in the past year [21,22,23,24,25,26,27,28,29,30].

Very few studies have investigated the mechanisms underlying impaired postural control in pure HSP. In a recent intervention study, we showed that hip adductor spasticity leads to impaired sideward stepping responses in response to external balance perturbations in patients with pure HSP. After botulinum toxin injections in the hip adductor muscles, participants showed improved reactive stepping responses [38]. In another intervention study in patients with pure HSP, we found a detrimental influence of calf muscle spasticity on postural responses to backward ('toes-up') balance perturbations and of calf muscle weakness on responses to forward balance perturbations [6]. Yet, in this latter study, botulinum toxin injections in the calf muscles did not improve the feet-in-place reactive balance responses of the participants [6]. In a parallel observational study, we were able to show that a general delay in postural responses to forward and backward balance perturbations may well be the main cause of balance problems, which is most likely associated with a slowed afferent conduction time through the posterior spinal columns [7, 30]. For this latter cause, no treatment exists other than the use of walking aids to provide mechanical support and additional sensory input through the upper extremities.

Unfortunately, the present data do not allow us to make any inferences on the effect of walking aids on falls. Still, many participants reported the use of different types of walking aids to increase their walking distance. At the same time, without a walking aid, 63% indicated that they could not walk at least 500 meters, while 28% were not able to walk at all. Besides walking aids, several participants used some type of ankle-foot orthosis or orthopedic footwear to improve their walking capacity, probably to prevent foot drag during the swing phase and/or optimize ankle stability during the stance phase. Based on the results of this study, it is not possible to conclude which walking aid and/or orthosis is generally most effective. Our experience has learned that a thorough individual clinical assessment, sometimes supported by an instrumented gait analysis, is the best way to provide an individually tailored advice for the use of medical devices. This advice should take into account both the gait pattern (e.g., foot drag, crouch, scissoring) and the execution of other daily life activities than upright standing and walking, such as stair climbing, squatting, cycling, driving a car etc. [31]. Several interventional studies have provided indications of improved gait capacity by robotic training [3], botulinum toxin injections in spastic calf muscles or hip adductors [8, 20, 33, 38], and intrathecal baclofen [27]. However, these studies mainly focused on gait speed and/or gait pattern as outcomes, and not on walking distance, performance of daily life activities, or falls. Studies on surgical interventions in HSP have not been conducted yet. Overall, it is fair to conclude that there is an urgent need for future studies in people with HSP that investigate the underlying mechanisms of their balance and gait problems and increased fall risk in order to develop novel and convenient intervention strategies to preserve life-long ambulatory capacity and gait-related activities, and prevent falls. Remarkably, even sitting for 30 minutes appeared to be a problem for 30% of the participants, which also necessitates further research in this field, particularly regarding wheelchair mobility.

### **Muscular and non-motor symptoms**

Unsurprisingly, muscle stiffness, muscle cramps and weakness appeared to be significant problems in our participants. Usually stiffness and cramps are treated with muscle relaxant medication, but apparently these symptoms are still very troublesome for many patients. Our results further showed that pain, fatigue, and autonomic problems are major (non-motor) symptoms in patients with pure HSP. Only few previous studies have mentioned pain as an important problem in this population [13, 25, 32, 36], even though chronic pain in the legs and/or back was reported by 72% of our participants. This number was similar to the reported frequency in previous studies [13, 36]. The nature of leg pain was most often described as nerve pain, cramping pain or restless legs. Back pain was most prevalent in the *lower* back. In our clinical experience, low back pain often has a continuous character, possibly related to postural deviation (i.e., anterior pelvic tilt with lumbar hyperlordosis). On average, the severity of pain yielded a median score of 4 on a numeric rating scale (0-10), but from a recent qualitative study we learned that, in individual patients, pain may



be severe enough to seriously affect their quality of life [25]. Besides chronic pain, many participants experienced chronic fatigue, both physically and mentally, scoring median severity scores of 6 and 5, respectively. From our recent qualitative study, it became clear that spasticity and muscle stiffness impact on physical fitness, while the high levels of attention needed to cope with balance and gait problems seem to cause mental fatigue [25]. Generally, chronic fatigue and pain are serious problems in many types of chronic neurological disorders such as stroke, Parkinson's disease, multiple sclerosis, and neuromuscular disease, which require specific clinical attention and treatment [5, 16, 19, 21]. Our results indicate that people with HSP form no exception to this rule, and probably remain undertreated in these respects. The present results confirm previously described micturation and defecation problems in people with pure HSP [23, 24]. As underlying causes for these problems our data indicate, on the one hand, extreme urge and problematic sphincter control [35] and, on the other hand, problems to reach the toilet in time. Whereas urological consultation is needed in the case of bladder and sphincter abnormalities, adequate treatment of spasticity and gait problems may be additionally helpful to reduce micturation and defecation problems. Sexual problems were also frequently mentioned by our participants. This result confirms a previous study reporting sexual complaints in 7 out of 11 patients with pure HSP, indicating pain and spasticity as most important underlying causes [24]. Hence, also for sexual problems, a combination of urological / gynecological consultation and adequate spasticity management seems to be crucial.

### **Predicting unsupported walking capacity and falling**

The duration of LLS symptoms appeared to be a strong predictor of being a faller. However, unexpectedly, people with an intermediate duration of LLS symptoms (6-10 years) showed the highest risk, much higher than those with a shorter duration (1-5 years), and also higher than those with a duration of more than 15 years. A possible explanation for this finding may be that in this stage of the disease (6-10 years) people are becoming increasingly affected by LLS related symptoms, while they are still trying to remain as active as possible in terms of standing and walking activities. This discrepancy might bring about an increased fall risk. In the next phase (11-15 years symptom duration), there seems to be a marked drop in fall risk, which might be related to a gradual adjustment of the activity pattern, increased carefulness, and the use of walking aids. Symptom duration longer than 15 years seems to increase fall risk again, perhaps due to the severity of the balance problems, affecting basic activities such as rising to stance, sitting down, and making transfers. Unfortunately, our data do not allow more detailed interpretation of the observed risk pattern, which warrants further investigation. Difficulty or inability to rise from the floor was another important risk factor of being a faller, which is an intuitive finding, as rising from the floor requires both sufficient lower extremity strength and basic balance capacity. Testing the individual capacity to independently rise from the floor

may, therefore, be an interesting clinical criterion to assess increased fall risk. The use of a wheelchair and the presence of non-neurological comorbidities appeared to be strong 'protectors' against being a faller. The remarkable result of non-neurological comorbidities being negatively associated with falling may be related to a lower level of standing and walking activities in these people, which may lead to a reduced fall risk. However, further research should shed more light on these findings.

With regard to walking, higher age was associated with a lower chance of being able to walk without aids for at least 500 meters, which probably results from a combination of normal ageing and disease progression. The observed odds ratio of 0.944 implies that, with every year, the chance of being a walker without walking aids decreases by a factor 0.944. Over 30 years, the chance of being a walker without aids would thus decrease to a mere 17.8% ( $0.944^{30}$ ). Experienced problems with gait-related activities also appeared to be a strong predictor of the inability to walk without aids. Lastly, the inability (or difficulty) to stand for 10 minutes and/or open a heavy door were also very strong predictors. This points towards the notion that standing balance capacity is an important prerequisite for independent walking. Asking patients in clinical practice whether they can easily stand for 10 minutes and/or open a heavy door may, thus, provide a good indication of their independent walking capacity. Again, further research should provide more insight in these relationships.

### **Strengths and limitations**

A limitation inherent in using questionnaires is the subjective nature of the results, which is why we emphasized that our data reflect the *experienced* complaints, activity limitations, and loss of motor capacities in people with HSP. Yet, experiences may reveal problems that remain unnoticed when focusing on objective measurements. Our study sample was limited in absolute numbers, which precluded subgroup analyses based on for instance genetic defect, or duration of LLS symptoms. Nevertheless, our study is the largest survey in people with pure HSP until now. In addition, our participants showed an equal sex distribution, wide age range, and a large variation in LLS symptoms, which supports their representativeness of the Dutch population with pure HSP, of which we probably included about 15% [11]. Since we excluded patients with complicated forms of HSP, our results cannot be generalized to the entire population with HSP.

### **Conclusion**

The results of this web-based survey indicate that people with pure HSP experience many physical complaints, activity limitations, and loss of motor capacities. Of these, muscle stiffness, problems with performing standing and walking activities, and increased fall risk are most prominent, but also pain, fatigue, autonomic dysfunctions, fear of falling, and problems with performing working and hobby activities are relevant symptoms and/or

areas of disability with an inherent loss of quality of life. Future research, using objective next to subjective measures, is needed to better understand the full functional impact of HSP on the daily lives of patients, to study underlying mechanisms of disabling symptoms, and to find new roads to interventions that are able to preserve balance and ambulatory capacity as well as limit the burden of the non-motor symptoms.

## **Declarations**

### **Ethics approval and consent to participate**

This study was approved by the regional medical ethics committee “Commissie Mensgebonden Onderzoek Arnhem-Nijmegen” (number 2016–2922) and conducted according to the declaration of Helsinki. All participants were adults who consented to participate with written informed consent.

### **Competing interests**

The authors declare that they have no competing interests.

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**CHAPTER 4**



# Identifying healthcare needs, expectations, utilization, and the experienced treatment effects in patients with pure HSP

Kerstens HCJW, Van Lith BJH, Nijkrake MJ, De Swart BJM, Van den Bemd LAC, Smeets RJEM, Fheodoroff K, Van de Warrenburg BPC, Van der Wees PJ, Geurts ACH. Healthcare needs, expectations, utilization, and experienced treatment effects in patients with hereditary spastic paraplegia: a web-based survey in the Netherlands. *Orphanet J Rare Dis.* 2021 Jun 24;16(1):283. doi: 10.1186/s13023-021-01915-0



## **Healthcare needs, expectations, utilization, and experienced treatment effects in patients with hereditary spastic paraplegia: a web-based survey in the Netherlands**

### *Background*

We aimed to identify healthcare needs, expectations, utilization, and the experienced treatment effects in a population of Dutch patients with hereditary spastic paraplegia (HSP).

### *Methods*

We distributed an online questionnaire among 194 adult persons with HSP in the Netherlands, of which 166 returned a fully completed version. After applying predefined exclusion criteria, 109 questionnaires from persons with pure HSP were analysed.

### *Results*

Healthcare needs and expectations were primarily focused on the relief of muscle stiffness and reduction of balance and gait impairments (65-80%), but many participants also expressed needs regarding relief of non-motor symptoms (e.g. pain, fatigue), emotional problems, impaired sleep and self-care capacity, and participation problems (> 60%). Remarkably, despite these frequent needs, relatively few participants (<33%) expected to be able to improve in these additional domains. Rehabilitation physicians and physiotherapists were more frequently consulted than neurologists and occupational therapists, respectively. Physiotherapy was the most often proposed non-pharmacological intervention (85%), followed by orthopedic footwear (55%) and splints (28%). Approximately one third of the participants was never offered any pharmacological (spasmolytic) treatment. Spasmolytic oral drugs, injections, and intrathecal baclofen were given to 41%, 26%, and 5% of the participants, respectively. Independent of the type of pharmacological intervention, 35-46% of these participants experienced decreased spasticity and improved general fitness. Other experienced effects differed per type of intervention.

### *Conclusions*

Based on this web-based survey in the Netherlands, there seems to be ample room for improvement to meet and attune the healthcare needs and expectations of people with HSP concerning both their motor and non-motor symptoms and functional limitations. In addition, the provision of adequate information about non-pharmacological and pharmacological interventions seems to be insufficient for many patients to allow shared decision making. These conclusions warrant a more pro-active attitude of healthcare providers as well as an interdisciplinary approach for a substantial proportion of the HSP population, also involving professionals with a primary occupational and/or psychosocial orientation.

Keywords: hereditary spastic paraplegia, spasticity, survey, patient-reported outcomes, needs assessment, healthcare utilization, experienced treatment effects

## Background

Hereditary spastic paraplegia (HSP) is a group of inherited neurological disorders characterized by progressive bilateral lower limb spasticity and muscle weakness [1]. Many complex forms of HSP exist, but in patients with 'pure HSP' the main neurological feature is a slowly progressive spastic paraparesis [2-4]. In a previous publication [5], we reported the first results of a web-based survey in the Netherlands, focusing on the spasticity-related complaints and activity limitations as experienced by patients with HSP. These data showed that patients with pure HSP experienced the greatest burden from muscle stiffness, physical and mental fatigue, leg and back pain, and limitations with regard to standing and walking activities. Furthermore, they reported a high frequency of walking aid use, fall incidents, and fear of falling. These findings are in line with the results of a previously published, qualitative study amongst persons with pure HSP [6]. Additionally, the participants in this qualitative study reported that they often missed the support from healthcare professionals in dealing with their spasticity-related complaints and activity limitations. More specifically, they expressed a need for personalized guidance and advice on how to adjust to the consequences of HSP in everyday life [6]. In their Cochrane review on multidisciplinary treatment following focal spasmolysis in people post stroke, Demetrios et al. stated that "using appropriate patient-centered outcomes of rehabilitations interventions with standardized measures may provide a more holistic picture" [7]. This was the reason to also include specific questions about healthcare needs, expectations, and utilization in the design of our web-based survey. In the present study, we focus on these specific questions.

Although similar healthcare aspects have already been investigated in an international survey of a mixed patient population living with more common causes of spasticity (e.g. stroke, multiple sclerosis, traumatic brain injury) [8], these issues have not yet been investigated in patients with inherited and progressive forms of spastic paraparesis. Furthermore, the experienced treatment effects reported in the abovementioned international survey were solely focused on botulinum toxin injections, not on pharmacological treatment in general.

Hence, in the present study, we report the data from our web-based survey addressing the healthcare needs, expectations, utilization, and experienced treatment effects amongst patients with pure HSP in the Netherlands [5]. The specific research questions were: 1) What needs do patients report regarding the symptoms and consequences of spastic paraparesis? 2) What treatment effects do patients expect at forehand? 3) Which healthcare professionals do they consult and how often? 4) Which interventions are proposed by their healthcare providers? and 5) What pharmacological treatment effects do they experience?

## Methods

### Study design and setting

An online survey was conducted between January 2017 and June 2017 in the Netherlands amongst community dwelling persons with HSP. The content of the survey aimed to identify the experienced consequences of living with inherited and progressive spastic paraparesis, as well as the experienced needs and expectations regarding clinical management. As the data on the experienced consequences have been reported in our previous publication [5], the current study focused on the healthcare needs, expectations, utilization and experienced effects regarding clinical management. The study was approved by the regional medical ethics committee “Commissie Mensgebonden Onderzoek Arnhem-Nijmegen” (number: 2016-2922), and conducted according to the declaration of Helsinki.

### Participants

Participants were recruited in three different ways. First, on our request, the national patient organization for neuromuscular disorders in the Netherlands (‘Spierziekten Nederland’; [www.spierziekten.nl](http://www.spierziekten.nl)) invited their members of the HSP working group by sending an email with information about the web-based survey. Second, all patients with pure HSP known at the expert center for rare and genetic movement disorders of the Radboud University Medical Center in Nijmegen were sent a letter with information about the survey. Third, all people to whom we reached out by either of the above-mentioned ways were asked to share their invitation with relatives suffering from HSP. All invited persons and relatives could then apply to participate by sending an email to one of the researchers (BvL). After receiving an email in which the person stated to be willing to participate, BvL sent a unique link to the web-based questionnaire to each potential participant. People were eligible if they were 18 years or older and had genetically confirmed HSP or, according to the recruiting researcher (BvL) and the senior author (AG), were very likely to have HSP based on their clinical symptoms and family history.

### Data collection

The structure and content of the survey were designed by a team of expert physicians, physical therapists, researchers, and persons with HSP, as described in our previous publication [5]. Part of the questionnaire (category D) was based on a previous international survey amongst patients living with spasticity [8]. This was extended with questions based on the findings from a qualitative study amongst patients living with pure HSP, who were interviewed about the daily life consequences of spastic paraparesis and related healthcare needs [6]. In addition, representatives of the national patient organization were consulted. The survey was sent to the participants using Castor electronic data capture (Castor EDC v2020.1.15).

The content of the survey was categorized in four categories: A. participant characteristics, B. complaints and activity limitations, C. loss of motor capacities, and D. healthcare needs and interventions. For the current study, only the categories A and D were used. The posed questions and the accompanying answering categories are listed in the additional file 1. To some extent, the amount of questions was variable for each participant, depending on their answer to a preceding question. Answering options were based on multiple choice, but some questions included a free entry format as one of the options. Completion of all questions took about 20 minutes, but there was no set time limit. Participants were allowed to pause during the questionnaire and continue at a later moment in time.

To ensure the inclusion of a homogeneous sample of persons with pure HSP, specific questions were included to identify patients with a complicated form of HSP and/or with neurological comorbidity.

### **Data analysis**

We excluded persons who confirmed that they had a complicated form of HSP (i.e. a genetic defect invariably associated with a complicated form of HSP and/or upper limb paresis, speech problems, cognitive disorders); or stated to have any neurological comorbidity that might interfere with spasticity, motor control, or physical fitness and activity. Furthermore, we excluded persons who reported that they suffered from spasticity for less than one year because of their limited experience with clinical management.

Data was exported from Castor into Excel files, which were imported into a statistical software program. Descriptive statistics were run in SPSS (IBM Corp. Released 2017, IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp).

### **Results**

A total of 194 invitations were sent to persons who were interested in participation, of whom 166 (86%) fully completed the questionnaire. After excluding 57 respondents based on the predefined exclusion criteria, a total of 109 (66%) questionnaires were used for analysis. Participant characteristics are displayed in Table 1. The mean age of the respondents was 52.8 years (SD 14.2). Fifty-seven persons (52%) had a known genetic defect, with SPG4 being the most frequently reported subtype (36/57=63%). Almost 50% of the participants had a disease duration of more than 15 years and more than 50% were unemployed, retired, or had a formally identified occupational incapacity. Almost 50% of the respondents reported micturation problems and used walking aids outdoors, whereas merely 12% was able to walk 100 to 1000 meters outdoors without walking aids. The degree of motor disability and autonomic dysfunction (e.g., bladder dysfunction) have been reported in detail in our previous publication [5].

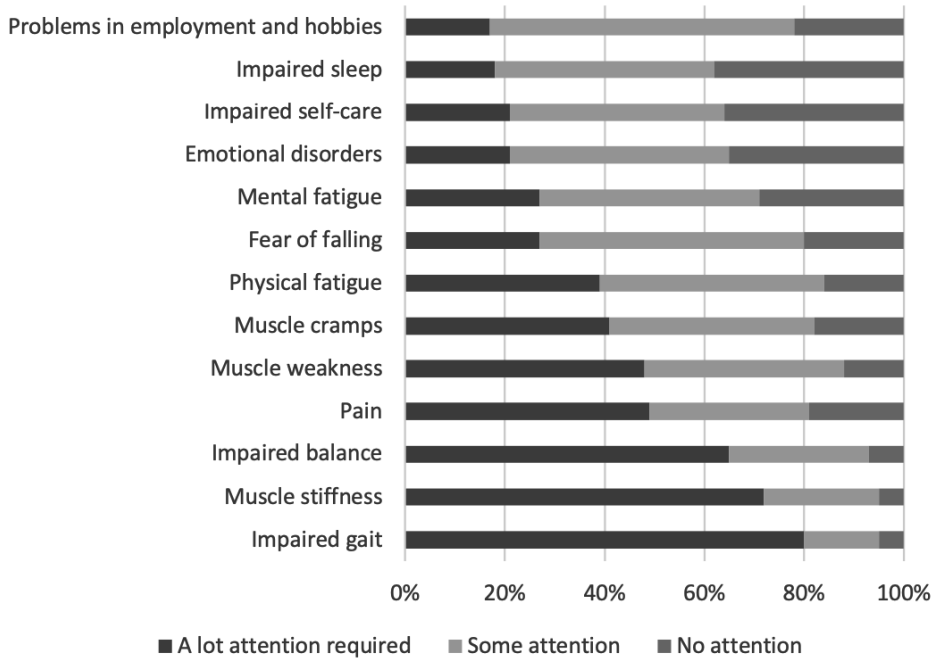
**Table 1:** Participant characteristics (N=109)

<b>Characteristics</b>	<b>n</b>
Sex (men/women)	54/55
Age in years (Mean (SD))	52.8 (14.2)
<b>Known genetic defect</b>	<b>57</b>
<i>SPG3a</i>	4
<i>SPG4</i>	36
<i>SPG5a</i>	2
<i>SPG7</i>	3
<i>SPG8</i>	3
<i>SPG10</i>	2
<i>SPG17</i>	1
<i>SPG31</i>	5
<i>SPG72</i>	1
Affected first-degree relatives	83
<b>Duration of spasticity symptoms (years)</b>	
<i>1-5 years</i>	21
<i>5-10 years</i>	21
<i>10-15 years</i>	16
<i>More than 15 years</i>	51
Micturation problems	49
Use of electrical wheelchair outdoors	29
Use of walking aids outdoors	50
Walking ability between 100 and 1000m without walking aids	13
<b>Non-neurological comorbidities</b>	
<i>COPD</i>	6
<i>Diabetes</i>	1
<i>Hypertension</i>	9
<i>Joint disorders</i>	13
<i>Cardiac problems</i>	4
<i>Other</i>	7
<b>Employment</b>	
<i>Full-time work</i>	27
<i>Part-time work</i>	14
<i>Self-employed</i>	8
<i>Student</i>	3
<i>Retired</i>	20
<i>Unemployed</i>	10
Occupational incapacity	27
Fully disabled (100%)	21
Mostly disabled (66-99%)	6

### Needs

Participants were asked to indicate the amount of attention (answering options: none, some, a lot) required during consultation with their physician for the healthcare needs regarding the experienced impairments and disabilities (see Figure 1). The majority of the participants (80%) prioritized gait impairments, followed by muscle stiffness (72%) and impaired balance (65%), all requiring “a lot of attention” (answering options see Figure 1). Other relevant topics were: pain, muscle weakness, muscle cramps, physical and mental fatigue, fear of falling, emotional problems, impaired self-care capacity, impaired sleep, and problems with employment and hobbies; all requiring minimally “some attention” in at least 60% of the participants.

Needs in terms of required attention during consultation for experienced problems



**Figure 1:** Participants’ needs in terms of required attention during consultation for their experienced problems (N=109)



## Expectations

The majority of the participants (63%) expected beneficial effects of the proposed interventions on gait (see Table 2). Other expectations, such as improved self-confidence, well-being, self-care, night rest, and reduction of pain and spasticity were less prevalent (<33%), as were expectations related to enjoying leisure time and hobbies, returning to previous routines, employment, perform simple tasks, or drive a car. In the free entry fields, four participants stated that they did not have any expectations of the proposed interventions, whereas two participants had the expectation that treatment would slow down the progression of their disease.

**Table 2:** Expected effects of proposed interventions (N=109)

Expected effect	% of participants
Improved gait	63
Improved self-confidence	32
Improved well-being	27
Enjoying leisure time and hobbies	26
Improved self-care	22
Returning to previous routines	20
Absence of pain	19
Improved night rest	15
Absence of spasticity	15
Being able to work	13
Better performance of simple tasks	12
Driving a car	9

## Healthcare professionals

Eighty-two percent of the participants had no or less than one consultation per year with a neurologist, whereas 16% visited a neurologist once or twice a year. The remaining 2% had three or more neurological consultations per year. As for consultations with a rehabilitation physician, 53% of the respondents had no or less than one consultation per year, 31% visited a rehabilitation physician once or twice a year, and the remaining 16% had three or more consultations per year.

Thirty-four percent of the participants had no consultations with a physiotherapist, 14% was treated by a physiotherapist once or twice per month, and 52% was treated more than three times per month. As for occupational therapy, 95% of the participants did not receive any consultations. Four percent visited an occupational therapist once or twice per month and 1% percent had more than three visits per month.

In everyday life, 49% of the participants did not need help from others, whereas others relied on the support from relatives (37%) or professional caregivers (12%). Two percent of the participants did not know how to organize support for the challenges they experienced in everyday life.

### **Proposed interventions**

Participants reported that a wide range of pharmacological and non-pharmacological interventions were proposed by their treating physicians (see Table 3).

#### ***Non-pharmacological interventions***

Physiotherapy was by far the most often proposed non-pharmacological intervention (81%), followed by orthopedic footwear (55%) and splints (28%). Sometimes coaching and support (e.g. psychological support and stress reduction), education, occupational therapy, social work, and fatigue management programs were proposed. Orthopedic surgery was proposed to only a small number of participants.

#### ***Pharmacological interventions***

Oral spasmolytic drugs (41%) were most often proposed, followed by intramuscular botulinum toxin (BTX) injections (26%). To a small number of participants (5%), the possibility of intrathecal baclofen administration (ITB) was proposed. A combination of pharmacological interventions was advised to 14% of the participants, whereas 38% reported to have not been offered any spasmolytic treatment.

Pharmacological interventions were mainly focused on reducing muscle stiffness, muscle cramps, and improving balance and gait. If pharmacological interventions were proposed, 72% of the participants were informed by their physician about possible side-effects. Insufficient information about the pros and cons of oral medication was reported by 27%. For BTX injections and ITB these numbers were 8% and 20%, respectively.

Before receiving an intervention, 43% of the participants was subjected to an instrumented clinical gait analysis (including 3-D motion capture for kinematics, force plates for kinetics, and surface electromyography for muscle activation patterns). To those who were proposed orthopedic surgery, instrumented 3-D gait analysis was performed in 69% of the cases.

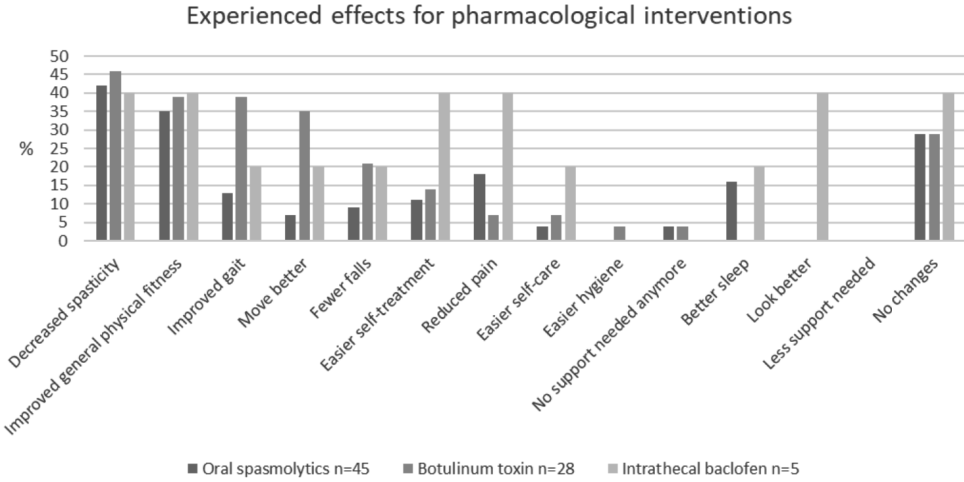
**Table 3:** Interventions proposed by treating physicians (N=109)

Proposed interventions by physician	% of participants
<b>Non-pharmacological interventions</b>	
Physiotherapy	81
Orthopedic footwear	55
Splints	28
Postural exercises	15
Massage	15
Psychological support	12
No intervention	10
Ankle-foot surgery	9
Hip surgery	4
Stress reduction	2
Education	2
Occupational therapy	2
Knee surgery	2
Social work	1
Osteopathy	1
Fatigue management	1
Lower spine surgery	1
<b>Pharmacological interventions</b>	
Oral spasmolytic drugs	41
Intramuscular botulinum toxin injections	26
Intrathecal baclofen	5

### Experienced pharmacological treatment effects

Figure 2 provides an overview of the percentage of participants that experienced specific treatment effects of pharmacological interventions. Independent of the type of intervention, 35-46% of the participants experienced decreased spasticity and improved general physical fitness. Other experienced effects differed per type of pharmacological intervention. Improved gait and movement was more likely to occur after treatment with BTX injections (35-38%), compared to oral drugs (7-13%) or ITB (20-25%), whereas pain reduction and easier self-care and self-rehabilitation were most likely after ITB (20-40%). The experienced effects on falls reduction were best for BTX injections and ITB (20-21%).

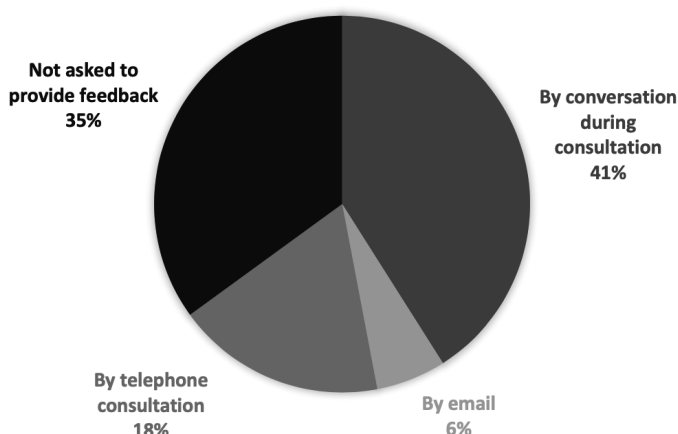
Sleeping responded best to oral drugs and ITB (16-20%). A substantial proportion of the participants experienced no effects at all from oral drugs (29%), BTX injections (29%), or ITB (40%).



**Figure 2:** Experienced effects of oral spasmolytics (N=45), botulinum toxin injections (N=28), and intrathecal baclofen (N=5).

Treatment with oral spasmolytic drugs was discontinued in 13% of the participants, mainly because of fatigue. Treatment with BTX injections was ceased in 7% of the participants, due to absence of effect. ITB was ceased in one of the 5 participants, because of too much muscle weakness.

The effect of the pharmacological treatment was mainly evaluated during the subsequent consultation with the treating physician. Thirty-five percent of the participants reported that they were not asked for feedback regarding the effects of the intervention. Figure 3 shows the frequency of the methods used for providing feedback about the effects of the pharmacological interventions.



**Figure 3:** Methods of providing feedback on treatment effect

## Discussion

This survey investigated the healthcare needs, expectations, and utilization regarding spasticity management in a sample of 109 persons suffering from pure HSP in the Netherlands. We found that needs and expectations were primarily focused on relief of muscle stiffness and reduction of balance and gait impairments. Yet, many participants also expressed a need for relief of pain, muscle cramps, fatigue, and fear of falling as well as reduction of emotional problems, self-care and sleeping problems, and problems with employment and hobbies. Notably, participants' expectations regarding the latter domains were less prevalent than their needs. As for the healthcare providers involved, rehabilitation physicians were consulted more often than neurologists, and physiotherapists much more than occupational therapists. Physiotherapy, orthopedic footwear, and splints were the most often proposed non-pharmacological interventions, whereas oral spasmolytic drugs were the most often administered pharmacological intervention, followed by intramuscular BTX injections. While both types of pharmacological intervention were experienced by participants to reduce spasticity and improve general physical fitness, improved motor control was deemed more likely after focal BTX treatment, whereas pain reduction and improved night rest were more likely to occur after systemic treatment (intrathecally more than orally).

## Healthcare needs and expectations

The participants' needs as observed in this survey are in line with the results of our qualitative study amongst 14 persons with pure HSP [6]. In the current study, we were able to quantify these needs, showing that 65-80% of the participants asked for a primary focus on relief of lower-limb muscle stiffness and reduction of balance and gait impairments. Nevertheless, many participants (> 60%) also expressed the need for substantial clinical

attention being directed at relief of pain, muscle cramps, fatigue, and fear of falling as well as a focus on improving societal participation and emotional well-being. Surprisingly, despite the fact that 49% of the respondents reported micturation problems (see Table 1), only 3% expressed the need of solving these problems. This apparent contradiction may be caused by the absence of a predefined answering option in the questionnaire. Therefore, in-depth exploration of individual patient needs – in conjunction with caregivers – may help to disclose needs in people with HSP that may otherwise remain unnoticed. In addition, because physicians and physiotherapists typically tend to pay more attention to sensorimotor symptoms than emotional and participation problems, our findings make a plea for a more interdisciplinary biopsychosocial approach to the clinical management of people with HSP, also involving professionals with a primary occupational and/or psychosocial orientation.

Remarkably, not many participants expressed expectations in the domains of non-motor symptom relief, self-care, returning to previous daily-life activities, or employment. This finding may be related to the fact that HSP is a progressive *inherited* disease [2] that forces patients to constantly adapt to slow increments in physical impairments and activity limitations. In this perspective, people with HSP are hoping to slow down physical deterioration rather than expecting improvement. This notion is supported by the finding that only 15% of our participants expected to ever be free of spasticity, while no more than 20% expected to be able to return to previous routines after treatment. These findings are in contrast to the results of an international survey amongst persons with various causes of *acquired* spasticity, such as stroke, multiple sclerosis and traumatic brain injury, of whom two thirds expected to achieve absence of spasticity [8]. This latter study also found a larger proportion of patients being treated with pharmacological interventions (73% BTX injections and 57% oral spasmolytic drugs) as well as more patients experiencing treatment effects (81% less muscle stiffness and 9% no effect). Apparently, there is a difference in expectations, proposed interventions, and experienced effects between persons with inherited progressive spasticity versus those with acquired chronic spasticity. Apart from the progressiveness of their spasticity, people with pure HSP have often witnessed relatives coping with progressive spastic paraparesis. Instead, people with acquired chronic spasticity, e.g., due to stroke, may have experienced regression of paresis and/or spasticity after disease onset. It is also possible that healthcare providers are more hopeful and willing to intervene in patients with acquired, non-progressive spasticity compared to those with inherited, progressive spasticity. Based on the current results and our clinical experience, we assume that the majority of people with pure HSP have rather realistic expectations with regard to effects of spasticity management, but are underinformed with regard to the possibilities of other forms of clinical management (e.g., occupational therapy, energy conservation management, psychosocial interventions, vocational advice). Our previous qualitative study has shown that – in this perspective – persons

with HSP ask for adequate information and coaching by their healthcare providers [6]. Healthcare professionals should incorporate this knowledge in their treatment approach.

### **Healthcare utilization and experienced treatment effects**

Rehabilitation physicians tended to be consulted more frequently than neurologists by our participants. This observation is probably characteristic of the Dutch healthcare system. In the Netherlands, the diagnostic phase of HSP is typically led by neurologists, whereas spasticity management largely takes place within rehabilitation teams supervised by rehabilitation physicians. More interestingly, only a few participants had consulted an occupational therapist, despite the fact that limitations in activities and participation were frequently reported. This is remarkable given the fact that occupational therapy is easily accessible in rehabilitation centers, hospitals and community practices all over the Netherlands. In addition, costs of occupational therapy are reimbursed by all Dutch health insurances. Probably, there is unawareness amongst people with HSP as well as amongst their treating clinicians of the services and solutions that occupational therapists can provide. A similar explanation may underlie the low rate of consultation by professionals with psychosocial expertise. In neurological conditions such as Parkinson or stroke, occupational therapy has proven to be effective [9, 10]. In their qualitative study in 2013, Grose et al concluded that persons healthcare professionals should be more aware of the emotional aspects of living with HSP [11]. We believe that our data justify more involvement of both occupational therapists and psychosocially oriented disciplines in the clinical management of people with HSP.

Of all interventions, physiotherapy was most often provided, but our data do not allow any conclusions regarding the content or experienced effects of physiotherapy. More than half of the participants used orthopedic footwear, which may be related to a higher risk of ankle-foot deformities and ankle instability associated with HSP [12]. Splints were used by more than a quarter of all patients, probably to support lack of foot elevation and to prevent tripping. Despite limited evidence in the literature [13] and a frequent lack of effects experienced by almost one third of the users in the current study, oral spasmolytic drugs were used by 41% of our participants. In contrast, an almost equal number of participants (38%) had never been offered any spasmolytic treatment. Of those who did use oral medication, almost one third felt underinformed. These results seem to point towards a pharmacological area characterized by a variable level of quality of evidence, and sometimes contradicting guidelines and recommended monitoring tools [14]. The figures on informed consent with BTX and ITB treatment seem to be slightly better, but inferences regarding their experienced effect compared to oral spasmolytic drugs cannot be made due to selection bias and the (very) small numbers of people on these more invasive treatments. Considering the type of treatment effect, especially participants with an ITB pump seemed to have a greater likelihood of experiencing pain reduction,

easier self-care and self-rehabilitation, and better sleep, whereas those who received BTX treatment seemed to have a higher chance of attaining improved motor control and capacity. But also in this respect, our results should be interpreted with caution.

Both the natural daily fluctuations in spasticity and the fluctuations induced by interventions such as botulinum toxin require careful communication between patients and healthcare providers to determine the optimal timing of (subsequent) interventions. Remarkably, more than one third of our respondents was not asked for any feedback on treatment results, whereas 41% was asked for feedback during subsequent consultations. To support patients in providing feedback, systematic monitoring of patient-relevant outcomes is crucial. It will help to tailor interventions to individual needs, to evaluate the effect of interventions, and to optimize timing [15].

### **Strengths and limitations**

A strength of this study is that we analyzed questionnaires from a relatively large group of people with pure HSP in the Netherlands, given the relatively low estimated prevalence of 800 persons with pure HSP in our country [16]. Our study sample also showed an equal sex distribution, a wide age range, and a large variation in duration of spasticity and underlying genetic defects, which underscores its representativeness for the Dutch population with pure HSP. As we included only participants with pure HSP, our findings cannot be generalized to people with more complicated forms of HSP. Another limitation is that our results cannot readily be generalized to people with HSP in other countries, given the differences in healthcare systems. However, since our results are in line with the findings of Grose et al, who studied the experiences of persons with HSP and healthcare professionals in England [11], we believe that a cautious use of our findings in the realm of Western European countries is warranted.

Another limitation is that only subjects without a positive family history or genetic diagnosis were checked for a formal diagnosis of pure HSP made by a neurologist. By including and excluding subjects based on specific questions, we tried to obtain a homogeneous sample with pure HSP, but it is possible that some people were incorrectly enrolled or excluded.

Our web-based survey was partly (category D) based on a previous international survey and extended with questions based on findings of a previous qualitative study [6] and input from representatives from the national patient organization. Yet, the involvement of healthcare professionals, who might have preconceptions regarding important aspects of HSP, might have biased its content. Furthermore, some questions allowed only dichotomous answers (yes/no), which might have influenced the relatively low scores for expectations regarding symptom relief (as participants could not indicate an expected



partial relief). The fact that answers were given in complete anonymity and without any time limit are considered strengths.

## Conclusion

Based on this web-based survey in the Netherlands, there seems to be ample room for improvement to meet and attune the healthcare needs and expectations of people with pure HSP. Besides relief of their motor symptoms and incapacities, they express a clear need to address non-motor symptoms and functional limitations, for instance regarding pain, fatigue, emotional problems (i.e., lack of self-confidence, fear of falling), impaired sleep and self-care, and problems with occupation and participation. In addition, the provision of adequate information about pharmacological interventions seems to be insufficient for many patients to allow shared decision making. These conclusions warrant a more pro-active attitude of healthcare providers as well as an interdisciplinary approach for a substantial proportion of the HSP population, also involving professionals with a primary occupational and/or psychosocial orientation. Regarding content of spasticity management in this population, there is a need for (inter)national guidelines, given the variety of clinical practice and the sparsity of clinical evidence. Hence, we recommend that future research aims at both improving spasticity management and broadening the scope of clinical management in people with pure HSP.

## Declarations

### Ethics approval and consent to participate

This study was approved by the regional medical ethics committee “Commissie Mensgebonden Onderzoek Arnhem-Nijmegen” (number 2016–2922) and conducted according to the declaration of Helsinki. All participants were adults who consented to participate with written informed consent.

### Competing interests

The authors declare that they have no competing interests.

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**CHAPTER 5**

# The perspective of patients with Stroke on spastic paresis

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Bert J. M. De Swart, Maria W. G. Nijhuis-van der Sanden,  
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## **Experienced consequences of spasticity and effects of botulinum toxin injections: A qualitative study amongst patients with disabling spasticity after stroke**

### *Purpose*

Chronic spasticity poses a major burden on patients after stroke. Intramuscular botulinum toxin injections constitute an important part of the treatment for patients suffering from troublesome focal spasticity. This study explores the experienced consequences of chronic spasticity amongst patients after stroke regarding physical impairments and activities, the experienced effects of botulinum toxin treatment on these domains, and whether current spasticity management addresses patients' needs.

### *Materials and methods*

Fourteen participants with chronic spasticity after stroke who were treated with cyclical botulinum toxin injections in the upper and/or lower extremity muscles were interviewed. Inductive thematic analysis generated representative themes.

### *Results*

Analyses of the interviews revealed three themes: 1) spasticity-related impairments and activity limitations; 2) fluctuations in spasticity related to botulinum toxin; 3) need for professional support and feedback. Besides motor impairments, participants experienced activity limitations in many domains of everyday life, with considerable day-to-day fluctuations. Moreover, treatment with botulinum toxin led to cyclical fluctuations in spasticity-related symptoms, which differed across participants. The participants called for shared responsibility for treatment, particularly regarding optimising the timing of injections.

### *Conclusion*

Incorporating patient-relevant outcomes into the current assessment of spasticity and monitoring these outcomes may improve spasticity management, particularly regarding the timing of botulinum toxin injections.

Keywords: stroke, spasticity, patient-reported outcomes, patient-generated health data, qualitative research, botulinum toxin

## Introduction

Although spasticity is a common and disabling impairment for many people after stroke [1], the patient's perspective on the functional consequences of spasticity has remained relatively neglected to date. In the literature, spasticity is typically characterised by muscle stiffness (both subjective stiffness and objective resistance against stretch), involuntary movement, muscle cramp, pain and fatigue [2, 3]. Personal factors (e.g. stress) and environmental factors (e.g. cold) often cause day-to-day fluctuations in the severity of spasticity [4] and, in the long term, spasticity may be complicated by changes in the soft tissue (e.g. muscle contractures) [2, 3]. Both pharmacological and non-pharmacological interventions aim to stabilise or reduce the functional consequences of spasticity by reducing muscle tone and maintaining joint range of motion [5]. Cyclical intramuscular botulinum toxin injections currently constitute an essential part of the treatment of troublesome focal spasticity [6]. In both research and clinical practice, however, the effects of such treatment continue to be measured primarily at the level of body functions and structures [7-9] according to the International Classification of Functioning, disability and health (ICF) [10]. Measurements of the consequences of spasticity in everyday life are much less common.

In most spasticity management studies, the (modified) Ashworth Scale and joint range of motion are set as primary study outcome measures [9]. In clinical guidelines [12], measures of bodily functions are recommended as well. Such measurements, however, do not provide any reflection of the problems that patients experience in daily life in terms of activity limitations and participation restrictions due to their spasticity [9, 11]. Hence, from a treatment perspective, it is questionable whether such measures of bodily function should dominate the evaluation and planning of cyclical botulinum toxin injections. Our clinical experience shows that patients with chronic spasticity after stroke tend to focus on much more personal aspects of their daily-life functioning. Such goals ask for outcome measures that assess their activity and participation level in addition to measures capturing bodily functions such as joint range of motion or muscle tone. Recent developments have shown the importance of involvement of patients in the development of Patient Reported Outcome Measures (PROMs) in an attempt to 'truly' assess the patients' perspective [13]. Not including PROMs in spasticity management could lead to a mismatch in expectations between clinicians and patients.

To address the issues outlined above, we explored the functional consequences of chronic spasticity as experienced by patients with stroke with regard to physical impairments and activities. We also investigated how they experienced the effects of botulinum toxin treatment on these domains and whether this treatment addressed their needs. We focused on individuals with chronic spastic hemiparesis after stroke who had received regular treatment with botulinum toxin injections for more than two years. The specific



research questions were: 1) How do participants experience the consequences of spasticity with regard to bodily functions and physical activities in daily life? 2) How do participants experience the effects of botulinum toxin injections on their physical impairments and activity limitations? 3) Does current spasticity management adequately address the needs of the participants?

## Materials and methods

### Design and setting

Between November 2016 and December 2017, a qualitative study, based on a constructivist epistemology, was conducted using semi-structured interviews to investigate the consequences of spasticity for everyday life [14]. In the interviews, multiple aspects of the participants' experiences were explored and interpreted in interaction with the interviewer. All interviews were held at the participants' homes.

### Participants

All participants were in the chronic phase after hemiparetic stroke. Additional inclusion criteria were: (1) being older than 18 years of age, (2) experiencing troublesome focal spasticity of the upper and/or lower extremity for more than two years, and (3) receiving cyclical treatment with botulinum toxin injections in the upper and/or lower extremity for more than two years. We arbitrarily selected a period of two years for the duration of troublesome spasticity, because sufficient experience with botulinum toxin injections was needed to be able to reflect on this treatment during the interviews. Exclusion criteria were: (1) insufficient command of the Dutch language, and (2) cognitive impairments (e.g. aphasia or amnesia) that might hinder independent reflection and effective communication during the interviews.

Participants were recruited from the clinical databases of two medical centres in a city in the eastern part of the Netherlands. We applied purposive sampling [14] to include a variety of participants in terms of age, sex, affected body side, years after stroke, and severity of hemiparesis. The rehabilitation physicians of both institutions approached and informed eligible individuals by telephone. Individuals expressing interest received an email containing additional information about the study. Patients who decided to participate informed the primary researcher (HK) by email. Following this notification, HK checked the inclusion and exclusion criteria and, after inclusion, planned an appointment for an interview at the participant's home. Written informed consent was obtained from all participants before the interview. Patients were allowed to withdraw from the study without giving a reason and without any consequences for their treatment. The study protocol was approved by the regional medical ethics committee (registration number 2015-2121). The procedures for data sampling, storing and reporting were in conformity with the Declaration of Helsinki [15].

## Data collection

All semi-structured interviews were conducted by HK, a trained interviewer and physiotherapist with more than 20 years of clinical experience in stroke rehabilitation. During each interview, HK was accompanied by a research assistant (CB, JD, LR, CJ, or TH). During approximately one-hour, participants reflected on the functional consequences of spasticity that they had experienced with regard to both physical impairments (e.g. stiffness, cramp, pain) and physical activities in daily life (e.g. sleeping, dressing, bathing, working). They also reflected on their experiences with the effects of the botulinum toxin injections that they had received, as well as on whether the current management of spasticity was adequately addressing their needs.

To ensure that all relevant topics were covered, an interview guide was developed [14] by HK with input from both clinicians (AG, MN) and researchers (TS, RN) working in the field of spasticity management and qualitative research, respectively. The duration of the interview was pre-tested on physiotherapy students. Subsequently, HK piloted the guide among two patients with chronic spasticity after stroke for face validity. Both patients were not included in our study. Findings from the first interviews were used to mould the interviews with subsequent participants. During the first four interviews, the spontaneous narratives of participants were slightly more directed at functioning of the lower extremity than towards functioning of the upper extremity. The interview guide was, therefore, adapted in order to ensure that ample attention was devoted to upper-extremity functioning during subsequent interviews. Moreover, the interviewer phrased questions based on the terms that the patients used regarding spasticity, if necessary. During the interviews, the research assistant wrote keywords from the participants' statements on sticky notes. This strategy was used to verify the interview content. It enabled the participants to correct possible misinterpretations immediately during the interviews and supported in structuring the interviews.

The planning of new interviews was stopped as soon as interim analyses revealed that no new information was obtained from subsequent interviews, indicating that data saturation had been reached [16] (see data analysis for more detail). The interviews were audio recorded and transcribed verbatim. Additional field notes were listed, as was the timeline with a visual representation of the spasticity-related physical impairments and activities (and changes in these areas). Personal identifiers were removed from the interviews, and a unique numeric code was assigned to each interview in order to guarantee anonymity.

## Data analysis

Analysis of the interviews followed the principles of inductive thematic analysis, as developed by Braun and Clarke. These principles follow the steps of becoming familiar with the data, generating initial codes, searching and reviewing themes and, finally,

defining themes [17]. The inductive approach allowed themes to emerge from the raw data through the process of open coding, without trying to fit the data into a pre-existing framework. The data were analysed using Atlas Ti version 8.1.27.0 (Scientific Software Development GmbH, Berlin, Germany).

After data collection from eight interviews, the interviews were coded by HK, who discussed the coding process and content with the second author (TS), an experienced qualitative senior researcher, until consensus was reached. Subsequently, HK grouped most codes into potential themes, which were then discussed with TS. The codes and content of the subsequent interviews were compared with the preliminary analysis, which was discussed with TS to assess possible saturation. When no new information was obtained anymore, three additional interviews were planned and analysed to strive for data saturation. The final version of the potential themes was discussed with all authors until they agreed to the final themes.

### **Trustworthiness**

Several strategies were applied to enhance trustworthiness, supported by the COREQ criteria for reporting qualitative research [18]. We took a variety of measures to respect the trustworthiness-related concepts of credibility (whether one can have confidence in the 'truth' of the findings), dependability (whether the data could be consistently repeated with the same subjects in the same context), confirmability (whether neutrality and accuracy of the data is respected), and transferability (whether the results could be transferred to other settings or groups) [19, 20]. We addressed credibility by recruiting participants with heterogeneous characteristics, with the goal of achieving a rich variety of experiences. Writing the keywords of the interview on sticky notes allowed participants to correct any misinterpretations during the interviews. Furthermore, the content and coding process were discussed first with TS and, later, with all of the authors. Dependability was enhanced by using a piloted interview guide, which ensured that similar relevant topics were discussed in all interviews. Confirmability was addressed by designing and discussing the content of the interview guide with all authors and using the findings of both pilot interviews for improving the focus of the guide. Combining the perspectives of the involved researchers, clinicians and patients enhanced neutrality and accuracy of the data. Transferability was achieved by describing participant characteristics, as well as through the processes of data collection and analysis.

### **Results**

The participants were fourteen patients with chronic spasticity after stroke. The participant characteristics are displayed in Table 1. Analyses of the interviews resulted in three themes: 1) spasticity-related physical impairments and activity limitations; 2) fluctuations in spasticity related to botulinum toxin; 3) need for professional support and feedback. The key messages from the participants are displayed in Table 2.

**Table 1:** Participant characteristics

N = Non-functional, F = Functional, UE = Upper extremity, LE = Lower extremity

Participant	Sex	Age (yrs)	Side of hemiparesis	Time post stroke (yrs)	UE-function	Capacity to walk	Injections in UE/LE/both
1	Male	59	Left	10	N	Yes	LE
2	Female	52	Left	4	N	Yes	Both
3	Male	66	Right	4	F	Yes	LE
4	Female	50	Left	6	F	Yes	LE
5	Male	66	Right	4	N	Yes	Both
6	Female	55	Left	6	F	Yes	Both
7	Male	71	Left	15	N	Yes	LE
8	Female	70	Right	19	N	Yes	Both
9	Female	42	Left	16	F	Yes	Both
10	Female	47	Left	4	F	Yes	LE
11	Female	39	Right	4	F	Yes	UE
12	Female	33	Left	28	F	Yes	LE
13	Male	67	Left	5	N	Yes	UE
14	Female	48	Right	5	N	Yes	UE

### Spasticity-related physical impairments and activity limitations

When invited to reflect on living with spasticity, participants expressed a variety of experiences. Similar descriptions were stated for problems regarding the functioning of upper and lower extremities.

Participants characterised spasticity in terms of increased tension in their limbs, stiffness, trembling and muscle cramping, which often resulted in the clawing of fingers and toes. These physical impairments caused problems in activities of daily life (e.g. dressing and walking). The execution of such activities was negatively influenced by stress in terms of time pressure or by being watched by others: *When I give presentations at work, I hold my arm, because the attention from the audience makes the cramps worse, causing my arm to rise' (P9)*. All of the patients reported experiencing abnormal posturing of the arms and legs. They expressed that loss of joint mobility in the affected ankle prevented them from taking normal steps with the non-affected leg. Many participants reported a flexed posture of the arm, wrist and fingers, which caused deformation of the limb. In addition to an unpleasant sensation, the abnormal limb posture limited the functional use of the hand: *I like to take flowers when I visit people. I can't do that anymore. The position of my fingers prevents me from holding them'(P8)*. Many participants reported that muscle length decreased over time, thereby reinforcing the abnormal limb posture and requiring further adaptation of movement patterns.

Participants described various sensations in their limbs that they associated with spasticity. Pain was mentioned by almost everyone. One patient complained that her leg felt like a wooden stick. Another participant talked about an itching sensation. Feelings of restlessness were reported as well: *'I don't know how to explain it. You don't see my leg moving, but I feel restlessness – a sort of "bzzzzz" – in my leg. I want it to stop' (P2).*

One very important experience related to spasticity concerned the loss of motor control. Participants felt instability in the ankle and foot during the stance and swing phases of gait. They reported a slow, small-stepped gait pattern with a tendency towards twisting the ankle, hyperextension of the knee and foot drag, which demanded considerable attention to adequate weight-bearing, foot positioning and walking: *'My leg doesn't go straight ahead when I'm walking. It always sweeps forward in a curve' (P3).* With regard to the arm, participants reported problems with positioning and with reaching for and manipulating objects. For instance, they fixated their affected arm under the safety belt when driving or used the non-affected arm to hold it while walking, in order to prevent it from 'floating away from the body'. When reaching and manipulating, they compensated for spasticity by maintaining an extreme focus on the task using visual control, as well as by generating excessive force to execute the movements. One participant reported that she was not able to prepare food unless she was alone in a quiet kitchen; otherwise, she would harm herself or drop the food.

Other major topics emerging from the participants' reflections on moving with spasticity included energy expenditure and fatigue. Performing normal activities required exceptional effort: *'Walking is truly an effort for me. I have to think about it. It doesn't just happen' (P10).* Many patients expressed chronic fatigue, which had gradually increased over the years. For some patients, the use of a cane decreased energy expenditure, thereby allowing them to walk for longer distances. One participant noted that, when her fatigue was too severe, she did not use her affected arm to load the dishwasher, as she was afraid that she would break the dishes.

Some participants expressed that they felt ashamed and inferior because of abnormal limb posture and movement: *'When I go outside, I always wear clothes with long sleeves so that people won't see the odd position of my arm. Yes, I'm vain' (P8).* Another participant recounted, *'I no longer ride a bike, because I'm not able to stabilise the handlebars and because my foot slips off the pedal. If I were to use a tricycle, people would see that I can't ride a bike anymore. That's embarrassing' (P3).*

## Fluctuations in spasticity due to botulinum toxin

Many participants felt that the very first botulinum toxin treatment resulted in greater relief than subsequent injection cycles did. At first, they often experienced a clear decrease in muscle stiffness and were able to move more easily. Yet, these benefits seemed to decrease over time. Participants searched for explanations for the attenuating effectiveness of the injections (e.g. a gradual increase in spasticity, loss of muscle length and the development of immunity to the botulinum toxin): *'The injections definitely don't work like they did at first. Then, it was easier for me to straighten my fingers. I think it's because of the increased spasticity and muscle shortening' (P9).*

In addition, for some participants, the period during which the symptoms were suppressed after the injections seemed to decrease with repeated injection cycles. This experience made some people have doubts concerning whether they should continue with the treatment, although most of them found it difficult to decide to stop the injections. Other participants wondered whether the effects that they experienced were due to the botulinum toxin or whether they were caused by habituation or co-interventions (e.g. the use of a splint). For this reason, they sometimes asked their physicians to delay the next injection cycle, in order to be able to disentangle the various influences.

Participants generally described three phases in the treatment cycle. Several days after the injections, they noticed that the medication was gradually starting to work. After this initial period, they experienced a more or less stable phase, during which the spasticity was maximally suppressed. This phase was followed by a gradual loss of effect, which typically took longer than the time it took for the medication to become effective. These phases were similar for both upper and lower extremities. The administration of repeated injections was timed and adjusted according to the experiences of both the physician and the patient. For most participants, the injection cycles were quite regular, as they preferred to plan subsequent injection cycles in advance, in order to prevent their symptoms from becoming too troublesome in daily life: *'At first, I would call to make appointments. I usually called too late, and then it would be several weeks before I received the injections. Now I have a fixed schedule. That works better' (P8).*

### ***The first phase of the injection cycle***

It took about 3–14 days for the participants to feel that the medication had truly become effective. Most participants experienced positive effects, such as decrease in muscle stiffness, trembling or cramps; improvement in the abnormal posturing of the arm, hand or foot; and, sometimes, improvement in motor control. Although the participants found it difficult to describe a specific sequence of effects, one clearly stated: *'The tension decreased first, and then the shaking. After that, walking improved' (P7).*

Several participants noticed improvements in the level of motor control over their bodies. Some of them indicated that increased stability on the affected leg prevented them from falling. One participant reported that, once the botulinum toxin started to work, it once again became possible to walk barefoot and climb stairs without an ankle-foot orthosis: *'If they can put a man on the moon, I ought to be able to go barefoot, right? That's really nice when it's 30°C or when I need to go to the loo at night. The injections make that easier again.'* (P2).

Some participants did not have to concentrate on walking as much after the injections, and this resulted in a higher level of societal participation. For example, one participant was able to walk to visit his daughter who lived three kilometres away, as he was less fatigued. Botulinum toxin also had a positive influence on how people felt. One participant noted: *'When the injections work, I can keep going. I can keep going like a normal person'* (P10).

All but one of the participants reported experiencing a reduction in pain after the injections. Other changes in sensation were reported as well. One participant observed, *'The first change that I feel once the injections start to work is the tingling in my leg'* (P4).

### ***The second phase of the injection cycle***

The participants discussed the second phase of the injection cycle only briefly. In this phase, the maximum effects were reached, and participants experienced their spasticity-related symptoms as 'stable' and relatively 'minor'. However, they all reported substantial day-to-day fluctuations in perceived spasticity. As noted by one participant: *'When the botulinum toxin injection in my arm is working, I am also able to walk better. I can simply walk to the bank'* (P13). This plateau phase lasted for around two to four months, although it varied considerably between participants.

### ***The third phase of the injection cycle***

After the plateau phase, the effects of the injections diminished. The positive changes experienced in the first phase gradually reversed. Participants provided several examples when talking about this phase. For example, they noted that muscle stiffness, trembling or cramps had returned in the arm, hand or foot, thereby making it more difficult to put on a hand splint or shoe. In some cases, an increase in finger flexion prevented them from wearing the splint. Pain, feelings of restlessness or pulling at the arm returned. Loss of leg motor control could lead to a decrease in walking capacity, deterioration of the gait pattern (e.g. hyperextension of the knee), requiring higher attention levels needed to avoid falling or injuries. One participant explained how her mood was influenced in this phase: *'When the injections wear off, my pain increases. One day is not a big issue, but several weeks.... That makes me grumpy, even to my loved-ones'* (P9).

As in the initial phase, it was difficult for participants to identify a sequence of changes in the wearing-off phase. As expressed by one participant: *'My fingers start to curl, and I have a strong pulling sensation around the wrist. Then it becomes harder to stretch my elbow, and I have more trouble putting on my hand splint. It depends on the situation. After having a few glasses of wine at a party, it just gets worse'* (P6).

## **Need for professional support and feedback**

### ***General support***

In general, the participants wanted to have shared responsibility regarding the selection of their treatment programmes, and be regarded as full members of their rehabilitation team: *'Exercises for my arm were prescribed without additional information about why to do this nor what to pay attention to. I did not feel taken seriously'* (P3). *'Nowadays, another physician provides the injections. At first, he followed a different injection procedure. After discussing this with him, he changed the procedure'* (P3). Participants expressed that they and their spouses should play an active role, ask for clarification when necessary and search for solutions: *'When I don't understand or agree with something, I pick up the phone in order to figure it out'* (P4). According to the participants, one crucial condition for shared responsibility was for their ideas and opinions on problem definition, goal setting and treatment to be heard, even though they were not experts in spasticity treatment. Despite their desire for shared responsibility, the participants realised that active participation is not possible for everyone, but that it should be customised to individual needs and possibilities: *'It doesn't matter to me, but other people might not be able to consider this. They need more guidance'* (P1).

The participants noted that easy and timely counselling from healthcare professionals was important to themselves, as well as to their relatives: *'When there's a problem, or if I want something, I can simply use WhatsApp to contact my therapist for treatment'* (P11). Smooth interaction with healthcare professionals, a good personal match and mutual trust were very important to participants in order to allow them to take an active role in managing their spasticity. They further identified the expertise of healthcare professionals as important. According to the participants, professionals should be familiar with both the disease and the treatment options. Based on their own experiences, however, not all professionals are familiar with interventions for reducing spasticity. For example, some participants had heard or read about botulinum toxin themselves and had therefore asked their physicians to refer them to specialists who would be able to administer this treatment. Others had discovered the possibility of receiving botulinum toxin injections by accident, after having been referred to specialised rehabilitation departments for a different intervention (e.g. functional electrical stimulation). Two participants complained about physicians who held conflicting opinions regarding injections in the arm or hand:



*'My doctor told me that an injection in my arm would be too complex. But my new doctor didn't have any doubts' (P10).*

### **Support related to botulinum toxin treatment**

The participants expressed a preference for low treatment frequency, and they were of the opinion that it was possible to optimise the timing of the injections. They assigned great importance to the timing of the injection cycles, as too much botulinum toxin in a short time period might cause an arm or leg to become too flaccid. With regard to the leg, participants usually preferred muscle stiffness to excessive muscle relaxation, so that they could continue walking: *'When my calf muscle is too relaxed, I can't walk at all. I'd prefer unpleasant stiffness in my leg' (P6).* Drawbacks of premature injections in the arm include a heavy feeling, shoulder subluxation and decreased motor control: *'The injection helps me, but it has to be very precise. When the injection is too early, the arm will feel very heavy, and the ball will slip out of the socket' (P8).*

The participants were aware that, in addition to the botulinum toxin injections, it was important to stretch the injected muscles regularly in order to prevent muscle shortening. They nevertheless found it difficult to maintain and dose the performance of stretching exercises (whether active or passive): *'When you do your best at school, you get an A. That's how I was raised: that's how to get where you want to be. But now, at times, the harder I train, the more my body will work against me. I've had to learn to listen to my body' (P10).* For this reason, the participants preferred to receive regular coaching and treatment from a physical and/or occupational therapist in the community, in addition to the self-guided exercises that they performed at home, in order to manage their spasticity. Many expressed that such professional support had been discontinued too early: *'After the outpatient rehab stopped, I no longer had any support. I needed cues for my everyday life, but I had to find out for myself' (P2).*

### **Feedback on spasticity-related problems**

Some participants periodically used diaries to monitor their symptoms, as they felt that it could help them to gain a better grip on their spasticity. When asked whether systematic self-monitoring of spasticity would be beneficial, some said that they did not need any systematic way of monitoring in order to notice that their walking had deteriorated. This subgroup nevertheless thought that some form of monitoring might have been helpful at an earlier stage, as a way to learn how to cope with spasticity. Most of the participants were willing to monitor their spasticity-related problems systematically for a longer period, if it would improve their ability to control their spasticity: *'Even after six years, I still notice that the spasticity changes. Monitoring could help to provide more insight into these changes' (P4).* Participants mentioned several outcomes they considered important: reduced pain and fatigue, improved motor control, and reduced activity limitations (e.g. regarding bare

foot walking, stair walking, cutting nails, and zipping a jacket). Participants hoped that regular feedback based on systematic monitoring would help them to maintain discipline in performing their self-exercises at home. They considered it important for such a tool to be easy to use, to take only a few minutes to enter the data, to consist of a few targeted questions and to provide a history profile of the data in a graph. They should also be able to provide healthcare professionals access to their data.

**Table 2:** Key messages from the participants

Theme	Category	Main message
Spasticity-related impairments and activity limitations	Stiffness	Stiffness, trembling and cramps cause problems in all domains of everyday life
	Posture	Abnormal posturing
	Pain and other sensations	Pain is an important consequence of spasticity
	Loss of control	Compensating for the loss of control demands additional attention
	Fatigue	Fatigue is a major problem
Fluctuations in spasticity related to botulinum toxin	Shame	Feeling ashamed and inferior, limits social participation
	General	The experienced effect of injections decreases over time First injection is the best one
	Phase 1	Injections result in a higher level of performing daily activities
	Phase 2	Only minor fluctuations of spasticity occur
Needs for professional support and feedback	Phase 3	The consequences of spasticity gradually reappear
	Call for general support	Patient and spouse should be informed Shared responsibility and decision-making should be customised to the patients' resources Healthcare providers should be familiar with spasticity management
	Call for support in issues related to botulinum toxin	Timing of injections is extremely important In addition to self-treatment, coaching from professionals is important
	Call for feedback	Monitoring spasticity helps patients to obtain a grip on spasticity and adhere to the treatment programme

## Discussion

Analysis of 14 semi-structured interviews of patients with chronic spasticity of the upper and/or lower extremity after stroke revealed three themes: 1) spasticity-related physical impairments and activity limitations; 2) fluctuations in spasticity related to botulinum toxin; 3) need for professional support and feedback. Participants experienced physical activity limitations in many domains of daily life. They often felt 'left to their fate' in this respect, and asked for support in dealing with the consequences of spasticity in everyday life. In addition to day-to-day fluctuations in spasticity-related problems, participants experienced large cyclical changes in their symptoms induced by the botulinum toxin injections. These cycles followed individual patterns. The participants expressed a need for shared decision-making, particularly with regard to easy access to professional support and the timing of the injections. Furthermore, they called for regular feedback in order to gain a grip on the consequences of spasticity and to maintain discipline in performing their self-exercises at home.

### Impact on daily life

Participants referred to the well-known impairments that are associated with spasticity, including stiffness, cramps and muscle pain [5]. In addition to these impairments, the participants reported that spasticity had a major impact on all domains of everyday living. These findings are similar to those based on the interviews that we conducted in patients with hereditary spastic paraplegia (HSP) [21], as well as to the findings of other studies involving neurological conditions (e.g. HSP, multiple sclerosis, or traumatic brain injury) [22, 23]. It is interesting to note that the stroke participants in the current study mentioned that spasticity was just one of several motor consequences of stroke, which implies that other symptoms contribute to the experienced motor problems as well. Participants told that they had somehow learnt to cope with spasticity, and that they could hardly remember how it had ever felt to be healthy. Some participants were embarrassed to reveal their limb deformities due to spasticity. Hence, healthcare professionals should be more aware of feelings of shame and embarrassment among their patients and explore whether they need psychosocial support to cope with these feelings. Although depressive symptoms are very common after stroke according to the literature [24], our participants mentioned no symptoms of depression, but we did not explicitly ask for symptoms of depressed mood.

Our study shows that, in order to address the impact of spasticity on daily life, healthcare professionals should incorporate more measures than just muscle tone and/or range of joint motion, thereby determining whether botulinum toxin is indicated or the condition of the patient requires follow-up. In a recent study, Baricich and colleagues (2018) demonstrated excellent reliability of a 15-item, 4-point questionnaire that assesses the extent to which spasticity affects functional capacities in real life (the Spasticity

Questionnaire in Real Life / SPQR). This questionnaire was based on the consensus of a panel of experts in the treatment of post-stroke spasticity [25]. The participants in our study reported similar activity limitations as reflected by the items incorporated in the SPQR (e.g. dressing, rising from a chair, walking, stair climbing, and preparing a meal). Yet, based on our results, the impact of spasticity would be captured even better when aspects regarding fatigue, energy expenditure, confidence and feelings of shame would be incorporated in the assessment, as these aspects often determine whether capacity is actually translated into daily life performance.

### **Gaining a grip on spasticity**

The participants reported having difficulty coping with the changes in spasticity that occurred during both the course of the botulinum toxin injection cycles and the day-to-day fluctuations. They wanted to have more insight in and control over both of these relatively unstable aspects of their spasticity. Some were uncertain with regard to the optimal starting time for and further timing of the botulinum toxin injections, as they feared (or noticed) that this treatment would (or had) become less effective over time. Such experiences of diminishing effectiveness over time may be related to the fact that subsequent injections were given before the effect of the previous injections had completely faded. This may have reduced the contrast between the experienced effects of subsequent injections, creating the illusion that the injections become less effective over time. Although participants had tried to find explanations for the aforementioned aspects themselves, they asked for professional and reliable information regarding these aspects.

In addition to receiving information, patients may be able to gain a better grip on spasticity by acquiring insight into their individual day-to-day fluctuations, along with the fluctuations induced by the botulinum toxin effects. The benefits of self-monitoring have been demonstrated in patients with other chronic conditions (e.g. chronic obstructive pulmonary disease and cerebral palsy). These patients were able to detect relevant changes in their health status [26], in addition to being able to reduce long-term complications [27]. Self-monitoring of spasticity could potentially help people with stroke to distinguish between day-to-day fluctuations and relevant changes in their health status, thereby supporting adequate and individualised timing of botulinum toxin injections. Improving precision in the timing of the injections by self-monitoring may also solve the assumed contradiction between planning injections in advance (to prevent symptoms from becoming troublesome) and postponing injections (due to fear of flaccidity caused too early administration).

Our study identified important content for self-monitoring from the patients' perspective. Sharing self-monitored patient reported outcomes as well as health data collected by professionals might improve the quality of spasticity management. The use of an online

monitoring tool could be useful to exchange relevant information amongst all parties involved. Because some participants felt that not all persons with spasticity are able to monitor their own spasticity levels, spouses, involved family members or physical therapists could contribute to monitoring the course of spasticity.

### **Shared responsibility**

Our participants called for partnership with healthcare professionals, as well as for education, coaching and customised interventions. Establishing partnership requires shared decision-making, which consists of providing information and supporting the decision-making process [28]. Mutual agreement on goals and interventions, along with the bond between patients and professionals may improve patient engagement and goal achievement [29]. In people with stroke, this demands a high level of skills on the part of healthcare professionals, given the possibility of stroke-induced communication problems and other cognitive disorders. If the patient and their caregiver(s) agree, caregivers could be involved in the process of shared decision-making.

Patient-reported outcome measures could help healthcare professionals to improve the tailoring of interventions to the specific needs of individual patients [30], in addition to potentially improving expectation management. Patient-relevant outcomes could probably be used to evaluate the effect of botulinum toxin injections as well.

### **Strengths and limitations**

This study has a number of strengths. First, we used the COREQ criteria for reporting qualitative research [18]. Second, we drew on the experiences of our previous study amongst persons with hereditary spastic paraparesis (HSP) [21] to acquire richer data in the interviews with the stroke participants. In the HSP study we started with a self-constructed interview guide. For the current study, this interview guide was adjusted and enriched with issues reported by persons with HSP in whom spasticity is the most cardinal feature and for which they are often treated with botulinum toxin. For example, persons with HSP mentioned the botulinum toxin dependent fluctuations of spasticity they experienced and this issue was, therefore, added to the interview guide for the current study. Third, the procedures for data collection and analysis were reviewed with the second and third authors, and ultimately with all of the co-authors. Fourth, we collected our data during interviews in the participants' homes, which created a comfortable and safe context within which the patients could share their experiences.

Limitations of this study included the fact that the participants were drawn from two specialised centres for the treatment of spasticity that were located in the same area in the Netherlands, which may limit their representativeness of the stroke population with spasticity at large. The participants were living in different parts of the Netherlands,

however, where they used local healthcare services in addition to the botulinum toxin injections that they received at one of the specialised centres. Furthermore, we did not include any participants with spasticity who suffered from severe cognitive disorders or aphasia, as this would interfere with our data collection. The latter limitation may impede generalisation to this specific subgroup of stroke patients.

## **Conclusion**

This study indicates that spasticity after stroke consists of more than impairments in bodily functions (e.g., stiffness, muscle cramps and reduced jointed mobility). Spasticity affects almost all domains of daily-life activities, including household, leisure and occupation. Healthcare professionals should be more aware of patient-relevant limitations in daily activities. When considering treatment with botulinum toxin injections, professionals should first inform and discuss the possible effects with their patients. Second, both professionals and patients need additional insight into the fluctuations that can occur during the injection cycle. Third, monitoring may help to identify the individual effects and duration of the injection cycle, as reported by patients. These three steps may enhance the active participation of patients in spasticity management, in addition to supporting self-management by understanding and providing a grip on the fluctuations of spasticity and improving the timing and customisation of interventions.

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**CHAPTER 6**

# Online monitoring of focal spasticity treatment with botulinum toxin in people with chronic stroke or hereditary spastic paraplegia: a feasibility study

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## **Online monitoring of focal spasticity treatment with botulinum toxin in people with chronic stroke or hereditary spastic paraplegia: a feasibility study**

### ***Background***

Spasticity management is complex due to multifactorial fluctuations in spasticity severity and functional impact. An online monitoring tool was developed to monitor these fluctuations over time in order to optimize focal spasticity treatment with botulinum toxin.

### ***Objective***

To investigate the feasibility and usability of an online monitoring tool amongst people with chronic stroke or hereditary spastic paraplegia (HSP) receiving botulinum toxin treatment and their healthcare providers (medical rehabilitation specialists and primary care physical therapists).

### ***Methods***

Mixed methods cohort study. Recruitment success was determined in three rehabilitation institutions (one academic). Adherence to the tool was measured across two cycles of botulinum toxin treatment. Usability was investigated quantitatively using the System Usability Scale (SUS), and qualitatively through interviews with patients and their healthcare providers. A deductive directed content analysis was used for the qualitative evaluation.

### ***Results***

Out of 161 unique consultations between December 2019 and September 2020, 43 participants (24 stroke and 19 HSP) were eventually enrolled. Recruitment success and adherence to monitoring were higher amongst peoples with HSP compared to chronic stroke. Usability was scored 'marginal' by rehabilitation physicians (SUS score 69), and 'good' by patients and physical therapists (SUS scores 76 and 83, respectively). The response rates for usability were rather low, respectively 60, 50, and 24%. According to participants, online monitoring may contribute to spasticity management if it is tailored to the actual needs and capabilities of patients, and if it can easily be integrated into the daily routines of all users.

### ***Conclusions***

Online monitoring of spasticity to optimize focal treatment with botulinum toxin seems to be feasible and usable. Tailoring the monitoring tool to patients' needs and capabilities, and active data sampling by professionals within their existing working routines are facilitators of clinical implementation.

Key words: Stroke, Hereditary Spastic Paraparesis, Spasticity, Feasibility studies, Internet-based intervention, Electronic health records

## INTRODUCTION

Although guidelines provide clear indications when to initiate botulinum toxin type A (BoNT-A) injections [1], the timing of subsequent treatment is challenging, because the severity and functional impact of spasticity as well as the fluctuations of symptoms over the course of time appear to be variable in many patients. Improved insight in these aspects by closely monitoring the consequences of spasticity may support decision making in spasticity management for both patients and healthcare professionals.

Spasticity is a prominent feature in many diseases of the central nervous system including stroke, traumatic brain injury, spinal cord injury and hereditary spastic paraplegia (HSP). It has recently been re-defined as 'disordered sensorimotor control resulting from an upper motor neuron lesion, presenting as intermittent or sustained involuntary activation of muscles'[2]. Pharmacological interventions aim to reduce the complaints and motor problems associated with muscle hypertonia and overactivity [1]. Where oral spasmolysis (e.g. baclofen, tizanidine) has a systemic effect on spasticity, BoNT-A is meant to exert focal effects in the injected muscles. Together with regular passive stretching of spastic muscles and (if possible) active exercises of their antagonists, BoNT-A injections are considered as a mainstay treatment in people who experience spasticity-related complaints and activity limitations [3]. BoNT-A injections temporarily (12-16 weeks) block the cholinergic transmission at the neuromuscular junctions, which is typically characterised by an initial phase during which the injections slowly become effective (1-2 weeks), a plateau phase with maximum effect (8-10 weeks), and a wearing off phase where the effects slowly decrease (3-4 weeks) [4].

Besides experiencing these slowly wearing on and off of the BoNT-A injections [5], people with spasticity may experience influences of personal and environmental factors such as fatigue, pain, emotional status, intercurrent medical conditions (e.g. bladder infection, constipation) and temperature changes [6]. People with potentially progressive (e.g. multiple sclerosis or HSP) or regressive (e.g. stroke, traumatic brain injury) disorders may also experience a gradual change in spasticity severity and impact, which makes decisions on timing, muscle targeting and dosing of BoNT-A treatment even more complex [7, 8]. For this study, we included both people with HSP and chronic stroke, as these groups represent populations with a different clinical presentation of spasticity (e.g. regarding progressiveness, upper extremity involvement, and severity of spasticity in relation to paresis) [9, 10].

Self-monitoring of spasticity severity and functional impact may potentially be helpful to support shared-decision making between people with spasticity and their healthcare providers and to improve the timing and execution of BoNT-A treatment. Indeed, the benefits of self-monitoring have been shown in several chronic conditions such as chronic

obstructive pulmonary disease and cerebral palsy [11, 12]. Therefore, we designed an online spasticity monitoring tool consisting of 1) a smartphone app (connected to an online platform) for patients to fill in a daily self-assessment to rate their spasticity-related symptoms and perceived activity limitations, and 2) an existing online physical therapy platform (Physitrack®) for healthcare professionals to read out the sampled data. The spasticity monitoring tool aims to provide optimal insight in the time course of individual complaints and activity limitations in order to empower self-management, shared decision making, and timing and execution of subsequent BoNT-A treatment. Besides the daily self-assessment, the online app provides several stretching exercises to be executed on a daily basis to prevent muscle shortening. Patient-relevant topics for the online app were identified through two qualitative studies in people with HSP or chronic stroke as well as through a nation-wide online survey amongst people with HSP in the Netherlands [7, 8, 13]. In addition, experiences and feedback from people with spasticity and their healthcare providers were used to improve the content of the online tool (app and platform) and tailor it to the needs of these users. The content of the online monitoring tool is explained in detail in appendix 1.

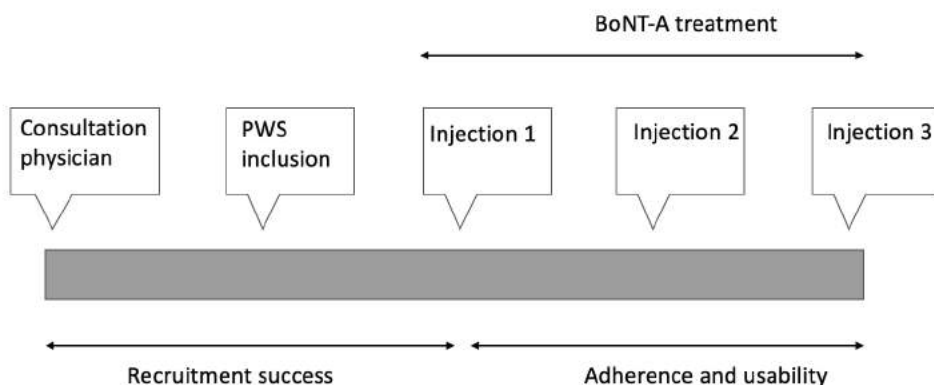
This study aimed to investigate the feasibility and usability of the developed online monitoring tool in people with HSP or stroke who already receive BoNT-A treatment. Specific research questions were: 1) what is the recruitment success for using the online monitoring tool in terms of number of enrolled eligible people in both groups? ; 2) what is the adherence in both groups to using the online app? ; 3) what is the usability of the online monitoring tool according to both groups and their healthcare providers (both medical rehabilitation specialists and primary care physical therapists)? ; and 4) in what way does the online monitoring tool contribute to spasticity management according to both groups and their healthcare providers?

## METHODS

### Design and setting

In this prospective multicenter cohort study, people with HSP or chronic stroke who were already on BoNT-A treatment for reducing spasticity-related complaints and activity limitations were eligible for inclusion. They were recruited through the outpatient clinic of three rehabilitation facilities in the Netherlands (Radboud University Medical Center, rehabilitation center Tolbrug, and the rehabilitation center of the Sint Maartenskliniek) between December 2019 and April 2021. They started using the online app immediately after they received their first, subsequent BoNT-A treatment and were followed up for two full cycles of BoNT-A treatment, which was a period of approximately 6 months, depending on the individual treatment cycle. A concurrent mixed methods approach was used to measure feasibility (quantitatively) and usability (both quantitatively and

qualitatively) (Figure 1). The study protocol was approved by the regional medical ethics committee (registration number 2019-5466). Data from the online spasticity monitoring tool was stored and reported according to both the Declaration of Helsinki [11] and the FAIR principles (Findable, Accessible, Interoperable, Reusable data) [14].



**Figure 1:** Study timeline. BoNT-A: Botulinum toxin type A; PWS: People with spasticity

## Participants

Three types of participants were included. People with chronic spasticity caused by either stroke or a pure form of HSP were eligible when they met the following criteria: a diagnosis of pure HSP or stroke ( $\geq 6$  months post onset), age  $\geq 18$  years, suffering from spasticity-related complaints and/or activity limitations, being already on BoNT-A treatment and scheduled for subsequent BoNT-A injections. Exclusion criteria were: inability to communicate in Dutch, cognitive impairments that might impact independent reflection on experiences with the online app during an interview (e.g., severe aphasia or memory deficits), not possessing (or being able to use otherwise) a tablet / smartphone or regular internet connection. The other participant groups consisted of the medical rehabilitation specialists (physicians) who were treating the included patients in the three participating rehabilitation facilities ( $n=8$ ), and the primary care physical therapists who were guiding the exercises of the people with spasticity in the home situation.

We aimed to include 25 persons with pure HSP and 25 persons with chronic stroke and all their involved medical rehabilitation specialists and primary care physical therapists.

## Recruitment procedure

During the consultation at the outpatient clinic, the medical rehabilitation specialists checked whether the persons scheduled for BoNT-A treatment met the inclusion criteria.



These people were then provided with written information about study goals and procedures and invited to participate. If a person, after a minimal reflection period of two weeks, was still interested to participate, the primary researcher (HK) called the patient by telephone to verify the inclusion criteria, provide additional information upon request, and answer any remaining questions. Prior to participation, all participants gave their written informed consent. They were all allowed to withdraw from the study thereafter, without giving a reason and without any consequence for their treatment.

After a person was included, the treating medical rehabilitation specialist was notified and requested to participate. In addition, when involved, the primary care physical therapist was informed about the study goals and procedures and asked to participate as well, but therapist participation was not mandatory for a patient being able to participate in the study. Both healthcare providers received written information about the study.

## **Study procedure**

All people with spasticity started using the online app on the first day after the first, subsequent BoNT-A treatment and stopped using the online app on the day of the third subsequent BoNT-A cycle. In this way, two full cycles of BTX treatment were captured (Figure 1). All people with spasticity received an individual username and password from the primary researcher (HK) to be able to enter data through the online app. Entering data into the online tool took approximately 2 minutes. The healthcare providers were informed that they had the opportunity to access the online platform of their patients at any time they wanted. They were provided with an individual username and password as well. All participants received both a digital and a paper version of the user manual of the online monitoring tool. In addition, they had the opportunity to contact a helpdesk by phone or email if needed. The helpdesk was available during office hours and responded to questions within one working day. One week after the first BoNT-A treatment, each person with spasticity was called by the helpdesk to verify that they were able to use the online monitoring tool and access the online platform as they wished.

## **Outcomes**

### ***Feasibility outcomes***

Feasibility was evaluated with the following quantitative outcomes: recruitment success, reasons for non-participation, and adherence to using the monitoring tool. Recruitment success and reasons for non-participation were assessed at three levels by calculating:

The proportion of people with spasticity invited for participation: the number of invited people was divided by the number of potentially eligible people; reasons for not-asking eligible people by the medical rehabilitation specialist were documented during the first outpatient consultation.

The proportion of people with spasticity that agreed to participate: the number of people that signed the informed consent was divided by the number of invited people; reasons for non-participation were documented by the primary researcher (HK).

The proportion of participating primary care physical therapists: the number of therapists that signed the informed consent was divided by the number of invited therapists; reasons for non-participation were documented by the primary researcher (HK).

Adherence to using the monitoring tool was calculated for a period of two botulinum toxin cycles: the number of completed daily self-assessments was divided by the expected number of self-assessments per person (i.e. the number of days included in the two consecutive BoNT-A cycles). Based on their adherence, people with spasticity were classified as a user (adherence >75%) or a limited/non-user (adherence <40%). These opposite groups in terms of adherence were identified to select patients for the individual interviews as described in the next paragraph.

### ***Usability outcomes***

After the third botulinum toxin injection, usability of the online monitoring tool was quantitatively assessed by all people with spasticity using the System Usability Scale (SUS). Usability amongst the individual medical rehabilitation specialist and primary care physical therapist was quantitatively assessed with the SUS after study completion of their last participating patient. The SUS is a subjective measure consisting of 10 questions, each using a 5-point Likert scale, ranging from score 1 (strongly disagree) to score 5 (strongly agree) [15]. The SUS is a validated measure for which a sum score (range 0-100) is considered 'unacceptable' when below 50, scores between 50 and 69 are considered 'marginal', and scores 70 or higher are considered to indicate 'good' usability [16]. In addition to the SUS, three self-constructed questions were asked to all participants: 1) 'Would you recommend the monitoring tool to other people with spasticity?' and 2) 'Would you recommend the monitoring tool to other healthcare professionals?' For these questions a 5-point Likert scale was used with the abovementioned scoring options. The third question ('Which grade of appreciation do you give the monitoring tool?') was answered using a 10-point scale (ranging from score 1 'unsatisfactory' to 10 'excellent').

Perceived usability for and contribution to spasticity management of the monitoring tool were qualitatively assessed through individual interviews. Because of the COVID-19 pandemic regulations during this study, each individual interview was conducted online (using the platform LifeSize®) instead of a face-to-face interview as initially intended.

Based on the adherence rates, we purposively sampled [17] nine persons with stroke or HSP from the user- and limited/non-user groups. In addition, all participating medical

rehabilitation specialists of the three centres involved (n=8) and all primary care therapists who returned the SUS questionnaire were invited for an individual online interview. Therapists who did not return the SUS questionnaire were called by the primary researcher (HK) to inquire whether they had used the monitoring tool. Those who confirmed they had used the tool were briefly asked to share their experiences concerning usability. Therapists who had not used the monitoring tool at all were briefly asked to mention the most important reason for non-use.

All individual interviews lasted approximately 30 minutes and were conducted by the primary researcher (HK) using a semi-structured interview guide. The interview guide was developed by the research team, and shared in advance by email with the participants to optimize their focus on usability topics [18]. The following topics were addressed:

1. To what extent is the tool suitable to monitor the time course of spasticity?
2. To what extent did the tool provide insight in the course of spasticity and the optimal timing of BoNT-A injections?
3. How did the tool impact on self-management and shared-decision making?
4. Which barriers and facilitators for using the tool did you experience?
5. Were the items of the self-assessment relevant for evaluating severity and functional impact of spasticity?

## Data analysis

Descriptive statistics were calculated for the feasibility outcomes and the quantitative usability outcomes. This analysis was performed using SPSS (IBM Corp. Released 2017, IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp).

The qualitative interviews were recorded, verbatim transcribed by a research assistant (MR), and imported into a software management package for the analysis of qualitative data (AtlasTi, version 8.1.27.0, Scientific Software Development GmbH, Berlin, Germany).

AtlasTi was used to perform a deductive, directed content analysis [19], which means that the transcripts were coded according to an a priori formulated theoretical framework of categories, which was based on the Consolidated Framework for Implementation Research (CFIR). The CFIR supports identifying potential influences on implementation in the five domains: intervention, inner setting, outer setting, individuals involved, and process of implementation [20]. After coding of the first transcript, the primary researcher (HK) and one of the supervisors (MN) discussed the content and coding process. After consensus, the second and third transcripts were coded, and discussed by both researchers. The ordering of the preliminary themes was initially discussed by HK and MN, followed by a discussion with the entire research team until consensus was reached on the final themes.

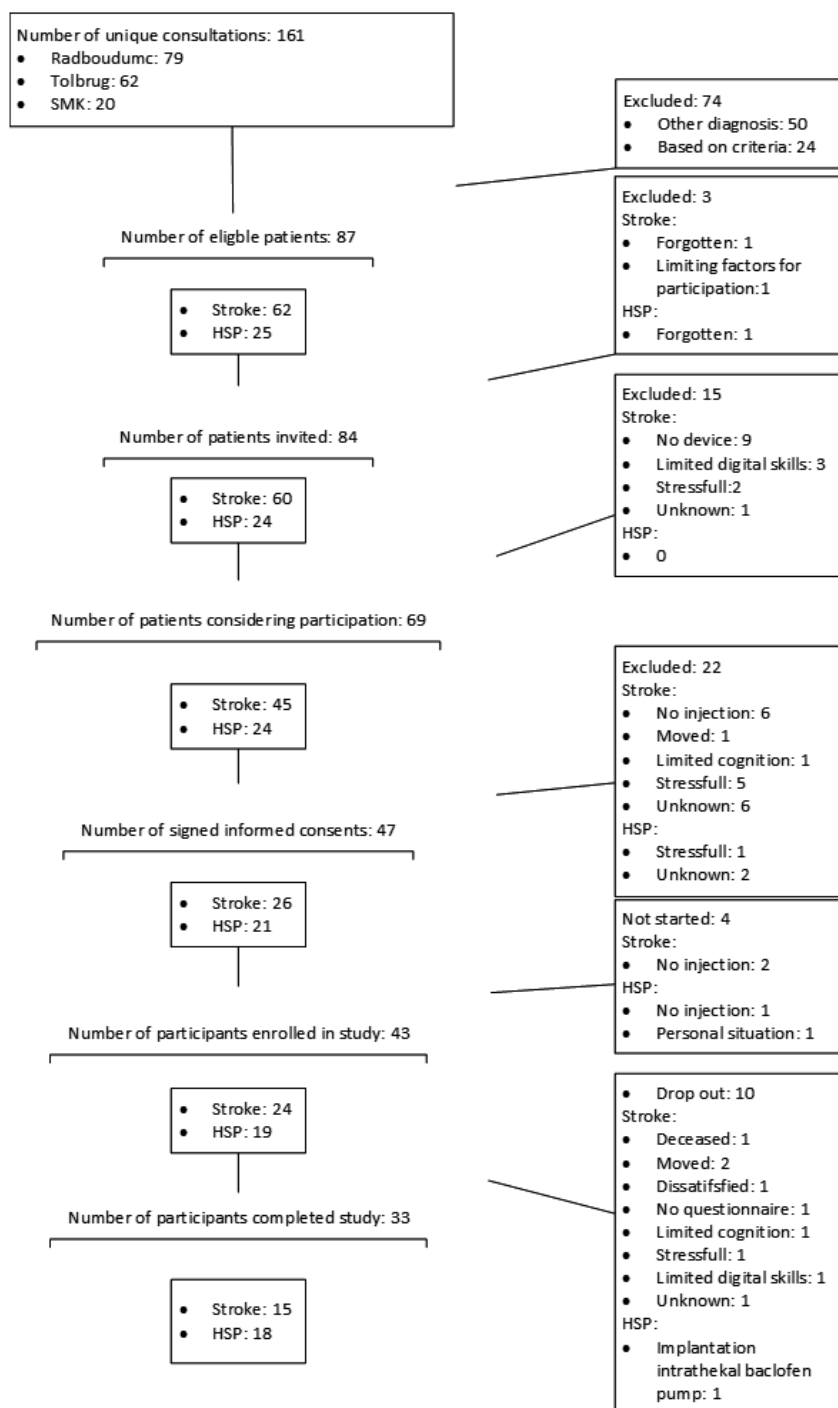
## Results

### Recruitment success

Between December 2019 and September 2020, 161 unique consultations of people requiring botulinum toxin treatment were recorded at the outpatient clinics of the three participating centres (Radboudumc n=79, Tolbrug n=62, and Sint Maartenskliniek n=20). Of these, 50 persons were excluded because they did not have a diagnosis HSP or stroke. Another 24 persons were not included because they did not fulfil the other inclusion criteria or because they met the exclusion criteria. Out of 87 eligible persons, 43 were eventually enrolled (24 stroke, 19 HSP) (see Figure 2). Their characteristics are presented in Table 1.

**Table 1:** Patient characteristics; n.a.: not applicable.

	<b>All patients (n=43)</b>	<b>Stroke (n=24)</b>	<b>HSP (n=19)</b>
Age in years, mean (range)	55.3 (24-77)	56.2 (32-77)	54.1 (24-72)
Sex (men/women)	25/18	13/11	12/7
Time post onset in years, mean (range)	13 (1-50)	9 (1-26)	17 (3-50)
Number of BoNT-A cycles before enrolment, mean (range)	13 (2-50)	14 (2-50)	13 (2-40)
<b>Treatment site</b>			
Radboud University Medical Center	24	5	19
Rehabilitation Center Tolbrug	13	13	0
Rehabilitation Center Sint Maartenskliniek	6	6	0
<b>Treated extremity</b>			
Upper extremity	10	10	0
Lower extremity	27	8	19
Both extremities	6	6	0
<b>Side of hemiparesis (stroke only)</b>			
Left		18	
Right		6	



**Figure 2:** Flowchart of participants from recruitment until completion of the study

Non-participation more often occurred among people with stroke compared to HSP for the following reasons: not having a suitable device, not knowing how to use a suitable device, participation being too stressful, and change of treatment plan.

Of the 43 participating people with stroke or HSP, 35 were consulting a primary care physical therapist, of whom 29 therapists (83%; representing 29 patients) were willing to participate. Reasons for non-participation of therapists were: increased workload (n=4), limited digital skills (n=1), or unknown (n=2). Of the 29 included therapists, 18 completed the study. Reasons for therapist drop out were patient drop out (n=9) or miscommunication (n=2). All eight medical rehabilitation specialists involved agreed to participate.

### Adherence to online monitoring

We intended to sample two full injection cycles, which would correspond to minimally six consecutive months. Unfortunately, directly after participant recruitment had started, the COVID-19 pandemic struck the Netherlands, which led to frequent postponement of BoNT-A injections. Rescheduling of appointments was not automatically communicated with the researcher, which caused that the monitoring window sometimes had started before the first injection and ended relatively early. Since we were interested in the adherence over a prolonged period, we decided to set the sampling period for every participant to 24 weeks, as this sampling period was used as a default by the online app provider. This strategy implied that a maximum of 168 daily self-assessments were collected per patient.

As depicted in figure 2, 33 patients completed the study (15 stroke, 18 HSP). Reasons for not completing the study were both frequent and variable in people with stroke, whereas only one person with HSP dropped out due to implantation of an intrathecal baclofen pump. The median overall adherence to using the online app in terms of number of completed daily self-assessments was 49%, which was higher for people with HSP (median 63%) than for people with stroke (median 20%) (Table 2).

**Table 2:** Adherence to using the online app

Overall (n=33)	Stroke (n=15)		HSP (n=18)	
Percentiles	25	0,20	0,03	0,33
	50	0,49	0,20	0,63
	75	0,77	0,61	0,90

## Quantitative results for usability

SUS response rates were 60% for people with spasticity (38% stroke and 89% HSP) versus 50% for medical rehabilitation specialist and 24% for primary care physical therapists (Table 3). Reasons for not using the online platform by medical rehabilitation specialists were: limited time / workload, technical problems, maternity leave / holidays, change of tasks, or misconception about the availability of the monitoring tool. Reasons for non-use by the other participants was not inquired for and thus remained unknown. From the participants that completed the SUS, people with spasticity scored on average 76 points, medical rehabilitation specialists 69 points, and primary care therapists 83 points. The majority of the respondents mentioned that they would recommend other people with spasticity and healthcare professionals to make use of the online app and platform.

**Table 3:** Usability scores for all groups of participants. SUS: System Usability Scale; Recommendation to other people with spasticity and to healthcare professionals varied from 'I fully disagree' (score 1) to 'I fully agree' (score 5); Overall grade for the monitoring tool varied from 'unsatisfactory' (score 1) to 'excellent' (score 10).

	All patients (n=26)	Stroke (n=9, 38%)	HSP (n=17, 89%)	Physicians (n=4, 50%)	Therapists (n=7, 24%)
SUS score (0-100)	75.6	72.8	76.9	68.8	82.5
Recommendation to other patients (range 1-5)	3.6	3.5	3.6	4	4
Recommendation to other healthcare professionals (range 1-5)	3.3	3.5	3.2	4.3	4
Overall grade for monitoring tool (range 1-10)	7.3	7	7.4	6.8	7.6

## Qualitative results for usability

Nine persons with spasticity (six with stroke, of whom three were non-users and three users, and three with HSP, all users), all eight medical rehabilitation specialists who recruited the patients, and six primary care physical therapists who completed the SUS were interviewed. From these interviews, a total of 291 unique codes were extracted and categorized into three themes: timing of monitoring, experienced benefits, and needs for improvement. Quotes (Q) of participants that exemplify the three themes are presented in table 4.

**Table 4:** Exemplifying quotes for the 3 themes. Q: Quote number, P: patient, Ph: physician, Th: therapist.

Quote number	Participant	Quote
Q1	P6	<i>'Although I have experience with spasticity for 15 years, I have to be aware not to make assumptions. Active monitoring helps me to detect changes I can relate to actual events.'</i>
Q2	Th11	<i>'The graphs are in line with my observations, but the patients' stories are more informative to me than the tool itself.'</i>
Q3	P6	<i>'Apparently, people think you either fall or you don't, but this is not true. When you would have asked me how often I stumble, you would have got a completely different answer.'</i>
Q4	P56	<i>'I valued that my physician had access to my graphs and the effects of treatment.'</i>
Q5	Ph1	<i>'I have become much more aware how difficult it is to capture these types of complaints, to make sense out of it by the patient and by myself . . . . . Actually, I would prefer to sample both a 'change-score' and a 'satisfaction-score'. After all, a 'change-score' can be low because everything is going fine, while at the same time a patient may express a high 'satisfaction-score'.'</i>
Q6	Th2	<i>'The patient and I, we felt we agreed on our findings. In case he rated an item with a 7, I would have scored a 7 as well.'</i>
Q7	P12	<i>'During the day, of course, I notice the consequences of my spasticity, but written down it is different, more confronting.'</i>
Q8	Th44	<i>'It would be good if all persons involved would be able to enter data into the tool. It would make it easier to evaluate and adjust spasticity management, when you have information from others as well.'</i>

### **Timing of monitoring**

People with spasticity had different thoughts about the usefulness of the online app. Some felt they did not need it, whereas others experienced clear advantages (Q1). In general, monitoring was experienced most useful at the start of the BoNT-A injections to establish the initial and subsequent need and timing of BoNT-A continuation. For some, monitoring at a later stage was considered redundant. This view was also expressed by some medical rehabilitation specialists. A more intensive information exchange at the start of the BoNT-A treatment would support adequate spasticity management in terms of indication and timing. One of the rehabilitation specialists suggested using the monitoring tool before the start of the BoNT-A treatment, thus creating a baseline that might help to assess the initial effects. Primary care physical therapists generally expressed a lower need for monitoring as they felt they had frequent contacts with the patients, providing them with 'a clear clinical picture' regarding the course of spasticity (Q2).



### ***Experienced benefits***

All people with spasticity valued the daily self-assessment, because they were better able to relate the fluctuations in the visual graphs of their symptoms and activity limitations to the timing of the injection cycles or to other spasticity influencing factors. One of them thought it would be better to ask for the frequency of stumbling than for fall incidents (Q3). Some medical rehabilitation specialists reviewed the online platform data before clinical consultation, which was valued by their patients (Q4). The experiences of the medical rehabilitation specialists themselves were diverse. Some reported that spasticity fluctuations were hard to associate with the injection cycles, sometimes due to missing values, whereas others expressed that use of the online platform clearly supported clinical decision making and shared responsibility between physicians and patients. One medical specialist reported the need for a satisfaction score besides a change score (Q5). Most primary care physical therapists were very pleased with the availability of daily stretching exercises through the online app. They were generally less focused on the use of the online monitoring platform. Their experiences with the online platform were diverse. Some did not use the online platform data at all, whereas others used it as a starting point for getting the clinical picture - based on the patients's narrative and physical examination - clearer. One therapist used the online platform data as a benchmark for his own findings to support spasticity management (Q6).

### ***Needs for improvement***

Some people with spasticity experienced the use of the online app as tedious. Moreover, they felt that the predefined symptom and activity scores were insufficiently tailored to their individual problems. A few persons stated that they were glad when the sampling period had finished, because it confronted them too much with their problems or because they were tired at the end of the day (Q7).

According to the medical rehabilitation specialists, important improvements would be: easier accessibility, better arrangement and adjustability of the visual graphs, integrated use of the data during the actual clinical consultation, and implementing individual treatment goals within the online platform data. Both medical rehabilitation specialists and primary care therapists mentioned that they would have appreciated the integration of the online platform with the regular electronic patient file, and the possibility to also add relevant data themselves to the patient's platform in support of shared decision making (Q8).

All participants would have appreciated personal face-to-face instructions instead of instructions by mail or telephone. They would also have liked to receive automatic notifications to support consistent use of the online monitoring tool.

## Discussion

The results of this study show that monitoring spasticity with an online tool is feasible and possibly useful for people with HSP. People with stroke typically experience more barriers with regard to using the online monitoring tool as their participation, adherence and response rates were much lower. Based on the patient responders to the SUS, the usability of the online app and platform would be good, but the large proportion of non-responders imposes a serious bias, particularly in people with stroke. The same is true for the therapist responders reporting high scores for usability. In contrast, the medical rehabilitation specialists all responded to the SUS indicating marginal to good usability. Qualitative analysis, however, still yielded many suggestions for improvement of usability of the online monitoring tool particularly from the perspective of patients and medical specialists. In their view, monitoring should be tailored to individual needs, integrated into the routines of all users, and be incorporated into the regular electronic patient files.

### Recruitment success and adherence

Recruitment success and adherence to online monitoring were much higher for people with HSP compared to stroke. Cognitive limitations and participation being considered too stressful accounted for a lot of non-participants with stroke. Cognitive impairments may also have played a role in the low adherence rates in people with stroke, while the higher adherence by people with HSP may be explained by the fact that we only included individuals with a pure form of HSP who typically have no cognitive impairments. The latter group may also have been more motivated, because spasticity is a key problem regarding their daily functioning and also shows a progressive character. In contrast, people with stroke often experience paresis and loss of muscle control to be the most dominant motor problems in terms of their daily functioning, while spasticity may be moderate or even regressive. In their systematic review, Block et al. showed that remote monitoring of physical activity across a variety of neurological diseases was feasible, even in people with impaired cognition [21]. Only a minority of their data showed no correlation between activity count and person-reported severity of symptoms. Reduced adherence was found in some of the included studies [21], but drop outs rates were lower than in our study. An important difference compared to the current study is that we used a device that automatically stored *but not sampled* data. Patients had to enter a daily self-assessment themselves, which was bothersome for some. Using individually tailored patient-relevant outcomes, which could be sampled by a well-tolerated device, may potentially increase adherence to online monitoring of spasticity, particularly in people with stroke.

### Usability and contribution to spasticity management

Regarding usability, our study showed SUS scores ranging from marginal (medical rehabilitation specialists) to good (people with HSP and stroke, and primary care physical therapists). The good scores of therapists may have been caused by the fact that the

Physitrack® app has primarily been developed for physical therapists and adapted to their working routines. In contrast, the medical rehabilitation specialists had to use the online platform next to their regular electronic patient file, which required additional time during the clinical consultations. Indeed the lack of integration of the online platform with the electronic patient file and the necessity to follow several steps to get access to the preferred visual graphs imposed an extra workload.

According to many participants, monitoring spasticity fluctuations is more helpful in an early stage of botulinum toxin treatment than in a later phase when individual treatment responses and spasticity fluctuations are better known to both patients and their healthcare providers. Nevertheless, even 'experienced' people with spasticity and BoNT-A treatment may face new situations in which it might be useful to intensify spasticity monitoring, for instance in the case of intercurrent co-morbidity, change of (oral) medication, or when the efficacy of treatment seems to attenuate. A temporary period of close monitoring of spasticity might help to adequately adjust spasticity management to the actual demands of the person. In people suffering from chronic obstructive pulmonary disease, cerebral palsy, or chronic heart failure, self-monitoring has shown to be effective in detecting relevant changes in health status [12], reducing long-term complications [11], and reducing healthcare utilization [22]. It is, therefore, likely that shared decision making in spasticity management can be improved when self-monitoring is used in critical periods of treatment, tailored to patient-relevant outcomes and combined with systematically sampled data by healthcare professionals.

Adopting a new element in spasticity management, such as online monitoring, requires that all users are convinced of the relevance and usability of the monitoring tool. For example, explaining the benefits of monitoring, matching expectations, sharing tips and tricks with 'super-users', may all contribute to adoption. To have the possibility of sending regular reminders, add background information, upload videos for movement analysis, put markers in graphs to identify important events, or zoom in and out of graphs by adjusting the timeline, may further add to the usability of online monitoring. Most importantly, monitoring should be incorporated in the daily routines of all users. Implementation of online monitoring should therefore carefully be prepared, for instance by analyzing the context of users and tailoring the intervention to individual needs and possibilities of users. Using the CFIR framework is helpful to identify potential barriers for implementation of a new intervention across multiple contexts [20].

### **Strengths and limitations**

Our study has several strengths. We tested the online monitoring tool in a realistic setting. The three participating rehabilitation facilities were allowed to follow their own protocols and workflows. In addition, we provided support by a helpdesk and called

people with spasticity one week after the start of data sampling, but we purposely refrained from sending regular reminders which would have influenced the spontaneous adoption process. A major study limitation is the selection bias that occurred due to non-participation, non-adherence, and non-response, particularly in the stroke population. In addition, we did not record participant characteristics or adherence for the medical rehabilitation specialists or primary care physical therapists. Moreover, these healthcare providers were able to consult the data entered into the online platform by people with spasticity, but they were unable to enter relevant data themselves due to the inherent technical limitations of the tool we used. This may have reduced their perceived relevance and usability and may have weakened the interaction between healthcare professionals and patients.

## **Conclusion**

Monitoring of spasticity-related symptoms and activity limitations by means of an online app linked to a commercially available online platform seems to be feasible and useful for people with hereditary spasticity (pure HSP) more than for people with stroke. Adequate individual user selection and focused timing of use, together with tailoring the monitoring to individual needs, integrating it into daily routines, and incorporating sampled data into regular electronic patient files may further improve usability and likelihood of clinical implementation.

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## Appendix 1: The online spasticity monitoring tool

The online spasticity monitoring tool consists of a smartphone app for patients, which included a daily self-assessment and a daily stretching exercise program), and an existing online physical therapy platform (Physitrack®) for healthcare professionals to read out the sampled data.

The online smartphone app provided people with spasticity the opportunity to rate their spasticity-related symptoms and perceived activity limitations daily. These data were automatically stored in the online platform, where they could be plotted as visual (timeline) graphs accessible for both patients and their healthcare providers through a personal and secured internet account. The visual graphs aimed to provide optimal insight in the time course of individual complaints and activity limitations in order to empower self-management, shared decision making, and timing and execution of subsequent BoNT-A treatment. Besides the daily self-assessment, the online app provided several stretching exercises to be executed on a daily basis to prevent muscle shortening.

### The online smartphone app

#### *The daily self-assessment*

- A. The daily self-assessment for persons with treatment of lower extremity spasticity (person with HSP, and persons with stroke) consisted of the following questions:
- How much are you bothered by:
    - Stiffness in your leg?
    - Muscle cramps in your leg?
    - Pain in your leg at rest?
    - Pain in your leg during movement?
    - Fatigue?
    - Fatigue after being active?
  - How satisfied were you with your gait?
  - How much have you fallen the last 24 hours?
- B. The daily self-assessment for persons with treatment of upper extremity spasticity (persons with stroke) consisted of the following items:
- How much are you bothered by:
    - Stiffness in your arm?
    - Muscle cramps in your arm?
    - Pain in your arm at rest?
    - Pain your arm during movement?
    - Fatigue?
    - Fatigue after being active?
  - How satisfied were you with your arm function?

- C. The daily self-assessment for persons with treatment of upper and lower extremity spasticity (persons with stroke) combined both abovementioned daily self-assessments.

The fall incidence was entered in numbers. All other questions were scored using an 11-point scale. Answer option zero represented no experienced problems, and 10 represented extremely bothered.

All data were visualised in a graph. As default setting, the individual items were grouped per date of entry. To increase understandability of the course of spasticity over time, items of choice could be selected and be presented as a trendline in the graph.

### ***The stretching exercise program***

A facultative daily stretching exercise program was incorporated in the online app. The exercises were focused on stretching of the spastic muscles of the upper, lower, or upper and lower extremity.

### **The online platform**

Data entered in the online app by patients were stored on the online platform and could be consulted by the individual patients themselves and their healthcare professionals.

All data were visualised in a graph. As default setting, the individual items were grouped per date of entry. To increase understandability of the course of spasticity over time, items of choice could be selected and be presented as a trendline in the graph. The timeline of the graph was neither adjustable, nor were the dates of botulinum toxin injections marked in the graph.







**CHAPTER 7**

# Summary and general discussion



The introductory chapter of this dissertation presented some quotes of a person with spasticity who had ‘to ride the waves’ of spasticity. These quotes underlined the struggle of people who are living with spasticity, and the complexity of spasticity management. This dissertation attempts to make this struggle easier by supporting personalized spasticity management through an online monitoring tool that is feasible and useful for people with spasticity and for healthcare professionals.

In this chapter, first a summary of this dissertation and its principal findings are given, followed by a general discussion. In the general discussion, the findings of three overarching themes: “Components of monitoring”, “Tailoring of monitoring”, and “Value of monitoring” are discussed. Next, some methodological considerations are addressed. Finally, the implications for future directions regarding research, education, and clinical practice are presented.

## Summary

In **Chapter one**, the rationale behind spasticity management and the purpose of this dissertation is described. Spasticity, a clinical symptom in disorders of the central nervous system such as stroke or hereditary spastic paraplegia (HSP), causes muscle overactivity as well as soft-tissue adaptations, creating a vicious circle of stretch-dependent spastic paresis. The level of spasticity may be affected by gradual changes (e.g. in progressive or regressive disorders) and temporary fluctuations (e.g. personal, environmental, and treatment factors). The functional consequences of spasticity depend on the demands and coping of the individual person.

Spasticity fluctuations, with their highs and lows, can be compared to the rising and falling of the sea tide, flood and ebb. During neap tide, the tide’s range between high and low tide is minimal because the inducing forces (gravity of the sun and moon) are partly neutralizing each other. Similarly, spasticity management asks for neap tide, in which the range between the highs and lows of spasticity is minimized. The main aim of an online monitoring tool would be to contribute to creating neap tide. Monitoring spasticity is challenging because of the inter-individual variety of the consequences of spasticity and its treatment. It also should support patient-centeredness in spasticity management, which implies shared-decision making, shared goal-setting, and self-management. The following three key-challenges were addressed: 1. Using patient-relevant outcomes, 2. Systematically sampling of data points over a prolonged time, and 3. Supporting shared-decision making, individual goal setting and self-management.

The first two phases of the “MRC framework for developing and evaluating complex interventions” were used to address the objective of the thesis by developing (phase one) and by testing, refining and assessing feasibility (phase two) of an online spasticity

monitoring tool. Evaluation and implementation (phase three and four of the MRC framework, respectively) lie beyond the scope of this thesis, but future perspectives on these topics will be given in the general discussion.

In **chapter two**, we explored the perspectives of people with pure HSP on spastic paresis through qualitative individual interviews. A thematic analysis of 14 interviews led to identification of four themes: “I stumble”, “I struggle”, “I feel ashamed”, and “I need support”. “I stumble” represents the experienced pain, stiffness, fatigue, impaired balance and gait, and day-to-day fluctuations of symptoms. “I struggle” refers to the attempts to adapt to the consequences of spasticity. “I feel ashamed” addresses feelings of fear and frustration, and the assumption of being judged by others. ‘I need support’ expresses the need for adequate information and interventions, competent healthcare professionals, and insight in the course of the disease and day-to-day spasticity fluctuations. In summary, we found that the participants were hindered by various (non)motor symptoms of spasticity that had considerable impact on their daily lives. The participants experienced problems in adapting to spasticity and asked for information, coaching, and support.

In **chapter three**, we conducted an online survey to quantify the experienced complaints, activity limitations, and loss of motor capacities, as well as to identify person characteristics associated with falls and walking capacities in a sample of 109 persons with pure HSP. These persons experienced a large range of impairments and limitations. Besides motor symptoms of spasticity such as muscle cramps and stiffness, nonmotor symptoms (e.g. pain, fatigue, and fear of falling) were experienced as a substantial burden of living with spasticity. Hence, besides the typical motor symptoms, nonmotor symptoms were considered potential items for monitoring spasticity and its functional impact. A univariate regression analysis was performed on the outcomes “being a faller” and “being a walker without aids”. “Being a faller” was positively associated with a longer duration of spasticity, whereas having non-neurological comorbidity and wheelchair use were negatively associated with being a faller. “Being a walker without aids” was negatively associated with a higher age, experienced gait problems, not being able to stand for 10 minutes, and incapacity to open a heavy door.

In **chapter four**, we used descriptive statistics on the quantitative data of the survey described in chapter 3 to identify healthcare needs, expectations, utilization, as well as experienced treatment effects in people with pure HSP. They asked for relief of both motor and nonmotor consequences of spasticity. Most beneficial effects were expected regarding gait. Relatively few participants expected to improve in nonmotor domains. Rehabilitation physicians and physiotherapists were frequently consulted by the interviewees. Approximately one third was never offered any pharmacological spasmolytic treatment. Pharmacological interventions were experienced to decrease spasticity and improve general physical fitness. Other experienced effects differed per type of

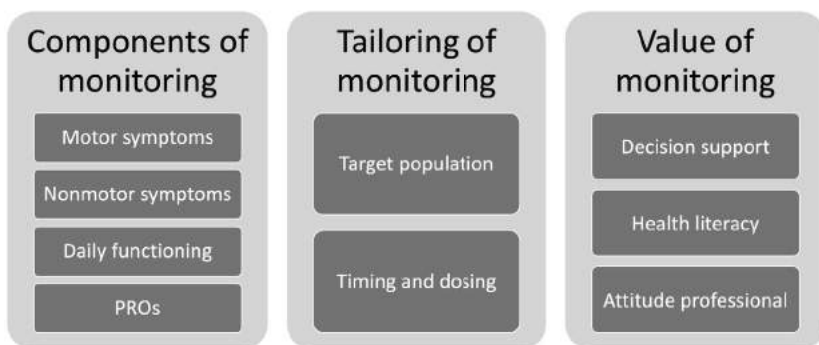
pharmacological intervention. Interestingly, although nonmotor symptoms of spasticity were regarded as a substantial burden (as shown in chapter three), the expressed needs for attention during consultation regarding these symptoms was relatively low. Also, the expected effects of proposed interventions regarding improved self-confidence, absence of pain, and improved night rest were low.

In **chapter five**, we investigated the perspectives on spasticity by qualitative interviews in 14 persons with stroke. In addition, we studied their experiences with botulinum toxin injections. Using an inductive thematic analysis, we identified three themes: “Spasticity-related physical impairments and activity limitations”, “Fluctuations in spasticity related to botulinum toxin”, and “Need for professional support and feedback”. “Spasticity-related physical impairments and activity limitations” refers to experienced muscle stiffness, abnormal posturing, pain and other disabling sensations, loss of motor control, fatigue, feelings of shame, and limited social participation. “Fluctuations in spasticity related to botulinum toxin” describes the experienced spasticity fluctuations during the botulinum toxin injection cycles. “Need for professional support and feedback” expresses the wish of the participants for adequate information, shared responsibility in the selection of interventions, optimized timing of botulinum toxin injections, and feedback to better cope with spasticity. Compared with the interviews with people with pure HSP, people with stroke experienced similar (non)motor consequences of spasticity and a similar impact on daily life. They expressed a need for information, coaching and support as well. Furthermore, people with stroke asked for partnership in intervention selection and optimizing the timing of botulinum toxin injections.

In **chapter six**, we used a mixed methods design to study the feasibility and usability of an online monitoring tool in 24 persons with stroke and 19 persons with pure HSP, eight rehabilitation physicians, and 27 primary care physiotherapists. The content of this online monitoring tool is described in chapter six as well. Descriptive statistics were used for the quantitative outcomes. A deductive directed content analysis was used for analysis of the qualitative data. Recruitment success and adherence to the monitoring tool were higher in people with HSP than in people with stroke. Rehabilitation physicians valued the usability of the online monitoring tool as “marginal”, whereas people with spasticity and physiotherapists scored the usability as “good”. Online monitoring of spasticity could be further improved if it were tailored to the actual needs and capabilities of patients, and if it were integrated into the daily routines of all users. This study showed different recruitment and adherence rates between the two patient groups, despite similar needs as expressed in the interviews of chapters two and five. Furthermore, the way of monitoring that was used varied between groups as well as the experienced benefits of the tool. Some people with spasticity found the tool supportive for spasticity management, whereas others did not want to be confronted with their impairments and limitations on a daily basis when entering data.

## General discussion

After clustering the principal findings and reflecting on the outcomes of the above-mentioned studies in relation to spasticity management, the following three overarching themes emerged: “Components of monitoring”, “Tailoring of monitoring”, and “Value of monitoring” (see Figure 1). These themes will be further elaborated in this general discussion. In addition, implications for clinical practice, research, and education will be given in the conclusion and recommendations section at the end of the general discussion.



**Figure 1:** Overarching themes for online monitoring of spasticity. PROs: Patient reported outcomes

### Components of monitoring

The definitions of spasticity according to Lance (1) and according to Pandyan et al. (2) put emphasis on the motor aspects of spasticity. In line with these definitions, clinical assessment of spasticity has always focused on these motor aspects (3). Indeed, the empirical studies presented in this thesis underline the importance of identifying the classical features of spasticity such as muscle stiffness and muscle cramps and their consequences for impaired motor control. At the same time, they emphasize that - from a patient perspective - non-motor aspects of spasticity should be addressed as well, such as pain, fatigue, sleeping problems, insufficient life balance, inappropriate energy management, feelings of shame and inferiority, fear and frustration. Furthermore, our studies have shown the importance of evaluating experienced activity limitations, which is in accordance with findings of Jacinto et al (4). Thus, in personalized spasticity management, clinically meaningful outcomes at activity and participation levels (5) that incorporate the perspectives of patients and caregivers (6, 7) are essential to evaluate the impact of treatment. From this perspective, a shift from a professional focus towards a more patient-centered assessment of spasticity is necessary.



However, examples of patient-centered (online) monitoring of spasticity are rare. Although some attention was given to non-motor symptoms and activity limitations due to spasticity in people with HSP (8-10), these aspects were neither identified in a recent systematic review on the management of HSP (11), nor are they incorporated in an instrument such as the Spastic Paraplegia Rating Scale (SPRS) (12). Non-motor impairments and activity limitations related to spasticity are also common in people with stroke but, in a recent systematic review of 28 papers regarding the effectiveness of botulinum toxin treatment for post-stroke spasticity, Andringa et al. (2019) almost exclusively identified outcomes related to motor impairments (5). In some other patient populations, questionnaires are used that do address the non-motor symptoms and daily life impact of spasticity, for instance the Multiple Sclerosis Spasticity Scale (MSSS-88). The MSSS-88 comprises three domains (spasticity specific symptoms, physical functioning, and emotional health and social functioning (13)), covering the above-mentioned non-motor and activity-related aspects, except fatigue. Such questionnaires may be valuable for spasticity assessment in other patients with upper motor neuron syndrome as well.

In an attempt to develop a patient-centered online monitoring tool that would cover a sufficiently broad scope of spasticity-related impairments and activity limitations, we incorporated patient reported outcomes (PROs) collected from our interviews into a short questionnaire that was integrated in the monitoring tool. To reduce the burden on patients, a selection of outcomes was made. Apart from the motor symptoms muscle stiffness and muscle cramps, we included the following non-motor and activity-related items: pain, fatigue, number of fall incidents, satisfaction with gait, and satisfaction with arm use. Yet, this extension still only partly covered the various aspects of living with spasticity as described by our patients during the interviews. In hindsight, the development of our questionnaire relied too much on a biomedical rather than a patient-centered perspective. Indeed, important elements of emotional health, daily-life activities and social functioning were not addressed.

Patient involvement is not only essential for determining the content of a monitoring tool, but also to ensure that patient-directed language is used for optimal communication and interpretation of the data. For example, a pilot version of our questionnaire asked about “scissoring gait” and “circumduction of the lower extremity” during the swing phase, but many patients did not understand this wording. Therefore, the questions were reformulated in the final version of the questionnaire. Another example of possible miscommunication occurred during the feasibility study. A male participant who explained that he had entered a low number of falls proposed that this specific question would be more valid and sensitive if it would ask for tripping or stumbling, because that is what happened to him many times a day. Hence, item selection and wording of the monitoring content

should preferably be based on a co-creation of all users, including patient representatives, to support patient-centered spasticity management.

The International Classification of Functioning, Disability and Health (ICF) can be used to categorize the consequences of spasticity over a range of physical, mental, and social aspects of health (14) and, thus, can support in the selection of items for a monitoring tool. The ICF defines health as “a state of complete physical, mental, and social well-being” (14). However, in 2011, Huber et al redefined health as “the ability to adapt and to self-manage in six domains: bodily functions, mental functions and perception, spiritual/existential domain, quality of life, social and societal participation, and daily functioning (15)”. This latter definition is much more suitable to the condition of many neurologically disabled persons and creates a good starting point to address the healthcare needs of these people. Yet, supporting the ability to adapt is easier said than done. To do so, healthcare professionals should be able to assess all relevant aspects of human functioning, coping, and acceptance. Prinsen and Terwee (2019) attempted to develop a single outcome to evaluate the ability to adapt, but concluded that the relevance, comprehensiveness, and comprehensibility of their questionnaire was still insufficient (16).

In summary, shifting to patient-centered spasticity monitoring requires a patient-centered, holistic approach towards developing a monitoring tool in which, next to bodily functions, other domains of patient-relevant health are incorporated. To achieve this, patients should be intensively involved in the development of the monitoring tool. Furthermore, healthcare professionals should be trained to support patients in developing skills to adapt to and self-manage the functional consequences of spasticity.

### **Tailoring of monitoring**

The target populations in this dissertation included people with HSP or stroke. Despite similar healthcare needs in these two populations, recruitment and adherence-to-monitoring rates were different. In chapter 6 we discussed several elements that might have contributed to these discrepancies, a.o. the likelihood of cognitive impairments in people with stroke, spasticity being the key characteristic of HSP versus just one of multiple sensorimotor impairments after stroke, and the progressive character of spasticity in people with HSP. Although we formulated inclusion and exclusion criteria to select participants who should be able to use the online monitoring tool, we did not screen their knowledge, attitude and behavior towards digital health interventions, which might have enhanced adoption of the monitoring tool (17). In 2021, Kloek et al. published a checklist to guide physical therapists in setting up personalized blended treatment, i.e. the integration of a digital application with traditional healthcare. Motivation, safety, equipment, digital skills, health literacy, self-management, time, and financial factors were all discussed with individual patients to explore their suitability for blended treatment (18).

During this session, information was tailored to the individual person's comprehension and communication skills. Explicitly discussing knowledge, attitude and behavior regarding digital health applications using a checklist and striving for comprehensive communication might have increased recruitment success, especially of our patients with stroke, as well as the adherence to using the online monitoring tool.

The observed discrepancy between our patient groups of similar needs versus different recruitment and adherence rates also raises the question how the functional consequences of spasticity should be monitored. Based on outcomes that are relevant for patients as reflected in PROs, Patient Reported Outcome Measures (PROMs) can be selected to assess these outcomes. PROMs can be generic, when relevant for all people, or disease-specific, when relevant for a specific group of people (19). In this perspective, it can be debated whether the non-motor and activity-related consequences of spasticity should be considered as disease-specific or generic. Remarkably, the variance in fatigue severity in people with a chronic disorder can largely be explained by transdiagnostic factors (e.g., pain, concentration problems, sleep disturbances, and limited self-efficacy) instead of disease-specific factors (20). For example, Wynia et al. (2006) showed that people with multiple sclerosis, Parkinson's disease, or neuromuscular disease experienced similar consequences of their disease at the levels of activity and participation, despite the existence of disease-specific impairments, a finding that was recognized by healthcare professionals (21). These studies seem to emphasize the importance of a holistic, transdiagnostic approach to spasticity management in which – at the minimum – generic PROMs are incorporated. On the other hand, our feasibility study showed that it is important to tailor monitoring to the individual needs of persons with spasticity. Insufficient tailoring of the questionnaire may have led to reduced adherence. The Canadian Occupational Performance Measure (COPM) is a personalized measure to identify goal achievement (and satisfaction herewith) in selfcare, productivity and leisure (22). The patient specific goal setting method has been developed in the Netherlands as a similar instrument to score activities to be used as an input for goal setting and evaluation (23). The patient specific functional scale (24) and the “patientspecifieke klachten” scale (PSK) are also used in the Netherlands (25) as self-reported outcomes of functioning in the field of physical therapy. They identify important personal activities and indicate how bothersome these activities have been during the previous week. Unfortunately, in our study, the technical specification of the online tool did not allow for incorporation of such personalized PROMs.

In summary, the characteristics of the target population and especially the needs and goals of the individual persons should be addressed in spasticity monitoring. Personalized measures such as the COPM and PSK can support in formulating and evaluating individual goals. Preferably, the selected PROMs evaluate the consequences of spasticity from a generic perspective if possible, and from a disease-specific perspective if needed. The use of personalized PROMs may help to enhance the adherence to monitoring.

A second important aspect regarding the tailoring of monitoring is the timing and dosing of data sampling. In people with chronic illness and disabilities, interventions have to address their changing needs over the lifespan, which asks for – on the one hand – timely and accurate assessment of experienced needs and – on the other hand – a minimally intrusive mode of monitoring that can be easily incorporated in their daily lives. In our feasibility study, we purposely requested participants to complete the entire questionnaire each day at a fixed time. Recently, sampling of experienced problems in interaction with ‘the real world’ has gained interest in several medical disciplines, as this would enhance the validity of the data (26). Real-world monitoring has also been advocated in the field of spasticity management after stroke (27).

A promising example of a method that uses real-world monitoring is “ecological momentary assessment”. In this approach, people receive a random cue, often through a mobile device, to report a momentary health outcome at unexpected time points. This mode of online assessment requires a minimum of time, reduces recall bias, and promotes ecological validity if sufficient data points are collected and interpreted over the course of time. Data can either be actively sampled by input from the participant, or passively by input from a wearable device. Based on this input, ecological momentary assessment can also prompt subsequent actions, for instance starting a relaxation app on a smartphone in the case of anxiety (26). In their systematic review, Yim et al. (2020) showed that smartphone-based ecological momentary assessments are feasible for people with depressive symptoms. Passive data sampling was useful for detection, prevention and treatment of depressive symptoms, leading to improved management of these symptoms (28). Neff et al. (2021) have used ecological momentary assessment in people after mild stroke and were able to show real-time associations between social interactions and post-stroke pain, fatigue, anxiety, and depressed mood (29).

Based on the above, it is reasonable to expect that also spasticity management may profit from ecological momentary assessment. Data sampling should specifically be applied well before and at the start of spasticity treatment to construct a baseline of the (experienced) consequences of spasticity. Discussing this baseline and the subsequent changes due to treatment effects will help people with spasticity and their healthcare professionals to get grip on spasticity and the initial treatment effects. Passive data sampling, for instance of daily-life activities and/or limb use, may improve feasibility, acceptability, and adherence to spasticity monitoring. When, after the initial phase, new data is used for timing of repeated interventions (e.g. botulinum toxin injections), the frequency of data sampling can probably be lowered. Currently, it is not possible to passively monitor muscle tone or muscle stiffness in a valid way, which hampers a passive collection of all data essential to spasticity management. This would, however, be a very relevant and promising area for future research.

## Value of monitoring

Ultimately, in order to be accepted and implemented, any monitoring tool will need to add value to patients and healthcare professionals involved in spasticity management. Both patients and healthcare professionals need to experience that – with the monitoring tool – they have more grip on the individual functional consequences of spasticity (and the fluctuations herein) and that shared-decision making in terms of selection and timing of interventions is facilitated. In chapter 6 we presented the experienced benefits of our online monitoring tool. Indeed, generally, participants perceived increased insight in the consequences of spasticity as well as in spasticity fluctuations and influencing factors. In addition, patients appreciated that physicians were informed about their condition before the actual consultation, and physicians felt that the tool might facilitate shared-decision making. Although these are important qualitative findings, the quantitative results indicated that not everyone made use of the monitoring tool, most likely because some participants did not yet experience sufficient added value. Particularly several physicians were hesitant to implement the tool due to practical inconveniences, whereas patients and physiotherapist were generally more positive in this respect. Importantly, almost all interviewed patients asked for partnership in spasticity management and wanted to be member of the treatment team, which calls for shared-decision making. Shared decision making implies that professionals and patients discuss the best available evidence and preferences, and that patients are supported to consider treatment options and reach an informed decision (30). Shared-decision making is particularly valuable in clinical areas with limited scientific evidence and a multitude of treatment options (31), such as in spasticity management. Using a monitoring tool that incorporates (personalized) PROMs potentially creates a good starting point for shared-decision making (32). Together with selected clinical outcomes, PROM-scores are able to shed light on the potential benefits and risks of different treatment options (33).

During the process of shared-decision making, patients need to actively participate in discussing the evidence, preferences, and treatment options, which requires sufficient health literacy. Nutbeam (2000) distinguished three types of health literacy: 1. functional literacy (i.e. basic reading and writing skills), 2. communicative literacy (i.e. cognitive and social skills to extract information and give meaning to it), and 3. critical literacy (i.e. cognitive and social skills to critically analyze information and use it for greater control) (34). Health literacy has been negatively associated with older age, cognitive impairments (35), and longer disease duration in a cohort of neurological outpatients (36). A lower health literacy hampers the understanding of information and the application of recommendations given by healthcare professionals and, thus, negatively affects shared-decision making. As mentioned before, in our feasibility study, we found remarkable differences in the recruitment and adherence rates between people with HSP and those with chronic stroke. Although both groups were asked to monitor the consequences of

their spasticity in an identical way, people with stroke showed a much lower adherence to the monitoring tool, which might have been due to a lower health literacy. A low health literacy, in its turn, may have been due to stroke-related cognitive impairments (36).

To improve health literacy, it is important to speak slowly, use non-medical language supported with pictures, limit the amount of information, repeat information and ask the patient to repeat it back, and create a safe environment (37). Regarding online monitoring, participants need sufficient 'electronic health (e-health) literacy', i.e. the ability to use electronic devices (38). In their systematic review, Kim and Xie (2017) argued that – apart from a good communication strategy to tailor e-health to the individual patient – education is needed to teach individual patients how to use information technology and e-health services (39). Face-to-face instruction and mutual exploration of the applied hardware and software features should be combined with instructions on data interpretation and (if applicable) required actions. In our studies, we provided written information in plain language augmented with instructional screenshots. Furthermore, we contacted participants by telephone one week after inclusion to check for residual questions and need for additional support. Possibly, face-to-face instructions and provision of a personal set-up and introduction of the monitoring tool might have helped to improve its use. Although – a priori – we identified the healthcare needs of people with spasticity through conducting interviews, a survey, and small pilot studies, our research team did not truly design the online tool in co-creation with patient representatives. Ideally, the online monitoring tool would have been a co-creation of people with spasticity, their healthcare professionals, and the research team.

As mentioned above, during the feasibility study, several healthcare professionals passed up the chance for creating partnership with their patients by systematic use of the monitoring tool. They expressed the following reasons for this lack of implementation: time pressure, the idea that monitoring has little added value in 'experienced' patients, and the belief that clinical observation was sufficient for decision making. Légaré et al. (2008) have introduced a taxonomy, including knowledge, attitudes, and behavioral factors, to study the barriers and facilitators for implementing shared-decision making in clinical practice from the perspective of healthcare professionals (40). Similar to our findings, they reported that time pressure, the lack of applicability due to specific individual patient characteristics, and the clinical situation (e.g. interference with usual consulting patterns) were barriers for implementation. As facilitators Légaré et al (2008) mentioned: professional motivation, and the belief that shared-decision making would have a positive impact on patient outcomes and the healthcare process (40). In our study, the healthcare professionals reported the following (additional) facilitators: the possibility to enter clinical observational data, good accessibility, integration of the tool in the electronic patient record, and incorporation of a self-rehabilitation module in the e-health

application. These suggestions from healthcare professionals imply that added value for them is not only related to shared-decision making and optimizing patient outcome, but also to optimization of the healthcare process itself.

Swinkels et al (2018) emphasized that – similar to patients – healthcare professionals need support for implementing an e-health application in clinical practice. According to their findings, professionals are in need of easy-to-use instruction materials, a help desk, and sufficient time to gain experience with the application. Furthermore, they requested support to integrate the e-health application in their regular workflow and electronic patient records (41). These needs are coherent with those reported in the systematic review of Schreiweis et al. (2019) (42) as well as with the findings from our feasibility study. Facilitating these practical issues will inherently increase the added value of a monitoring tool as experienced by healthcare professionals.

## **Methodological considerations**

In this thesis, we used the first two phases of the MRC framework for developing and evaluating complex interventions: the development (phase 1) and feasibility testing (phase 2) of an online spasticity monitoring tool (43). Although we did no formal implementation study (phase 4), in the feasibility study of chapter 6, we used the Consolidated Framework for Implementation Research (CFIR) to identify potential influences on implementation in five domains: intervention, inner setting, outer setting, individuals involved, and process of implementation (44). We further used elements of a design-thinking framework in the process of developing and evaluating the online spasticity monitoring tool. Design thinking is a systematic innovation process in which the needs of the end-users are explored, a variety of scenarios to solve those needs are developed, after which rapid prototyping is used to test and optimize scenarios in a real-life context. This ‘doing-to-think approach’ helps to rapidly discover unforeseen challenges and unexpected consequences, so that these can be addressed or alternative scenarios can be chosen (45). Using these three frameworks helped to develop and evaluate the online spasticity monitoring tool in an iterative process among patients, healthcare professionals and the research team. As a consequence, the providers of the online platform and the app provider (two separate companies) had to swiftly react to the feedback of potential users. Unfortunately, the online platform provider could not keep up with the speed of this process and, additionally, suffered from internal technical and organizational problems. This is why we had to continue our feasibility study only with the online app provider, who was able to provide a web-based platform as well, albeit less sophisticated than that of the initial platform provider. As a result, only the patients who used the app were able to enter data, whereas healthcare professionals could only read out these data. As mentioned above, this situation may have reduced the added value of the online monitoring tool for these professionals.

In the development phase, we deliberately started with identifying the healthcare needs, expectations, and experiences of people living with spasticity and their healthcare professionals by conducting semi-structured interviews, instead of performing a systematic literature review. Although we gathered rich information from these target groups, it is possible that we neglected already existing information on this topic. Further, we attempted to strengthen the voice of users by step-wise participant selection. In several small pilot studies directed at optimizing the content of the monitoring tool before starting the feasibility study, the selected patients could only participate in one study. We also held various feedback sessions with healthcare professionals to learn about their needs, experiences, and expectations. In hindsight, the focus of these sessions was more on the content of the tool than on the mode of operation or the features of the interface of the online platform and app. Ideally, we would have involved potential users also in these respects, but the provider of the initial online platform was not really able to implement any operational suggestions.

In the feasibility-testing phase, we conducted a mixed methods study using a sequential explanatory design. Combining qualitative with quantitative methods helped us to interpret the quantitative results and better understand the participants' views (46). The feasibility study was not only executed in our university medical center, but also in two regional rehabilitation centers. While one academic physician was involved in the development phase of the monitoring tool, all other physicians were not and could, thus, provide entirely 'independent' feedback. In order to study the feasibility in a real-world context, we did not put any restrictions on how to use the online monitoring tool, neither did we send reminders to use the tool, except for one standard telephone call to each involved participant one week after inclusion to inquire about possible start-up problems. Unfortunately, this real-world context was complicated by the organizational consequences of the COVID-19 pandemic in each of the participating clinics. During the study period, our research team tried to support participation in the feasibility study by providing help desk support on request, meanwhile taking care not to increase the load on any group of participants. Providing more guidance by regular contact between the research team or the help desk and the participants might have increased adherence rates, but these numbers would probably not be predictive of real-life implementation.

## **Conclusion and recommendations**

This dissertation contributed to more personalized management of spasticity. First, experiences and needs of people with HSP and stroke who are living with spasticity were identified. Second, online monitoring of spasticity was shown to be feasible and potentially able to provide relevant insight in the individual course of spasticity, supporting shared-decision making. Finally, insight was obtained in important barriers and facilitators for using an online monitoring tool in spasticity management, providing



direction for further improvements. These improvements are essential to increase the clinical value of online spasticity monitoring not only for people living with spasticity but also for their healthcare professionals. To facilitate the next steps, I would like to end with specific recommendations for improving spasticity management within the three academic domains: clinical practice, research, and education.

### **Clinical practice**

First, healthcare professionals should tune to the level of (e-)health literacy of individual patients to ensure proper communication and shared-decision making. Second, individual goals should be determined before initiating treatment and evaluated after (initial and subsequent) treatments, preferably with personalized PROMs. Third, patients and healthcare professionals should tailor the intensity of spasticity monitoring to individual patients' needs, thereby taking into account the phase of the treatment process. Fourth, online spasticity monitoring should be integrated in the work process of healthcare professionals as much as possible, preferably in the regular electronic patient records. Fifth, online spasticity monitoring should be regarded as an integral element of the treatment process that is able to improve patient outcomes.

### **Research**

Regarding research on spasticity management, the following recommendations can be made. First, based on PROs, a coreset of generic PROMs should be developed to optimize patient-centered monitoring and treatment across patients with different upper motor neuron syndromes. Second, the content of the monitoring tool should be able to assess the ability to adapt, besides capturing the actual situation. An instrument to measure the ability to adapt is currently not available and should, thus, be developed. Third, for a valid assessment of the current situation regarding the functional consequences of spasticity in which data are actively and/or passively sampled at random points in time, the feasibility and efficacy of "ecological momentary assessment" should be studied in people living with spasticity.

### **Education**

With regard to education on spasticity management, healthcare professionals (and students) should learn to pay attention to the patients' perspectives on living with spasticity. They should learn to focus on goals and outcomes that are relevant to individual patients and support shared-decision making based on these goals and outcomes. Furthermore, they should be trained to consider spasticity management from a holistic perspective, which requires an interdisciplinary approach. This can be facilitated by interdisciplinary education.

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Starboard

Port

Nederlandse samenvatting

List of publications

Curriculum vitae

PhD portfolio of Hans C.J.W. Kerstens

Research Data Management

Dankwoord





*“De ene dag loop ik heel beroerd, maar de dag daarna zien mensen mij lopen en denken ze: waarom is zij nou arbeidsongeschikt? Er is toch niets met haar aan de hand? Dat is lastig, heel erg moeilijk om mee om te gaan.”*

*“Er was een stukje moeder, een stukje echtgenote, een stukje Ineke de werkneemster. Ik was goed in wat ik deed, en wat ik deed vond ik leuk. Met een vingerknip werd dit anders. Mijn sociale activiteiten en netwerk zijn weggefallen. Ik ben nu ongewenst huisvrouw. Mijn arm is spastisch en mijn been heeft een clonus. Lopen is voor mij een werkwoord geworden, het gaat niet meer vanzelf. Door de injecties met botuline hoef ik niet meer zo na te denken. Helaas werkt dat maar acht weken. Daarna kantelt mijn voet weer en overstrekt mijn knie.”*

Het dagelijkse leven is voor veel mensen met spasticiteit een worsteling. Daarnaast is de behandeling van spasticiteit voor zowel patiënt als zorgverleners complex. Dit proefschrift tracht bij te dragen aan het verminderen van die worsteling en heeft als doel het verbeteren van de persoonsgerichtheid van spasticiteitsbehandeling door het ontwikkelen van een online monitoring tool die geschikt is voor zowel patiënten als zorgprofessionals. Deze samenvatting geeft een beknopt overzicht van de uitgevoerde studies in dit proefschrift en de resultaten ervan, en geeft aanbevelingen voor het verder verbeteren van de behandeling van spasticiteit-gerelateerde problemen in de toekomst.

**Hoofdstuk 1** beschrijft de theoretische achtergrond van spasticiteitsbehandeling. Spasticiteit is een symptoom van verschillende aandoeningen van het centraal zenuwstelsel, zoals een beroerte of hereditaire spastische paraparese (HSP). Spasticiteit veroorzaakt, naast onwillekeurige musculaire overactiviteit, ook veranderingen in de spieren en andere weke delen, waardoor geleidelijk een vicieuze cirkel ontstaat van toenemende spasticiteit, spierstijfheid en spierverskorting. Naast toename van spasticiteit, kunnen er ook tijdelijke fluctuaties optreden in de mate van spasticiteit op basis van persoonlijke, omgevings-, en behandelactoren. Eén van de behandelactoren wordt veroorzaakt door injecties in de spier met botulinetoxine. Dit medicijn blokkeert tijdelijk de signaaloverdracht tussen zenuw en spier waardoor de overactiviteit van de spier tijdelijk vermindert. Het medicijn moet langzaam inwerken, en na een periode van optimale werking, raakt het weer uitgewerkt zodat er weer een nieuwe injectie noodzakelijk is. In hoeverre de spasticiteit iemand belemmert in zijn of haar leven hangt af van de mate van spasticiteit, de invulling van iemands' leven en de manier waarop het individu omgaat met de gevolgen van spasticiteit.

De fluctuaties in de mate van spasticiteit zijn te vergelijken met het optreden van de getijden, eb en vloed. Ze treden welhaast onvermijdelijk op. Maar tijdens doortijd is de rijzing van de zee (het verschil tussen eb en vloed) minimaal, omdat de aantrekkingskracht van de maan en zon elkaar grotendeels neutraliseren. Het in kaart brengen van de fluctuaties

in de spasticiteit kan inzicht geven in het korte- en lange-termijn beloop van spasticiteit. Dit zou gedaan kunnen worden met behulp van een online monitoring tool. Het doel van een dergelijke tool is het bijdragen aan het creëren van doeltijd: het minimaal houden van de fluctuaties in de spasticiteit, hetgeen de grip op het fenomeen voor zowel patiënt als zorgverleners zal verbeteren. Met andere woorden, monitoring kan de persoonsgerichte behandeling van spasticiteit bevorderen. Aanvullend hierbij zijn aspecten zoals gezamenlijke besluitvorming, het formuleren van doelen, en zelfmanagement belangrijk.

Binnen het in dit proefschrift gerapporteerde onderzoek hebben wij een tool voor de online monitoring van spasticiteit-gerelateerde problemen op systematische wijze ontwikkeld middels het "MRC-raamwerk voor het ontwikkelen en evalueren van complexe interventies". Na de ontwikkeling (c.q. de eerste fase) van het raamwerk werd in de tweede fase de haalbaarheid van de tool bepaald in de praktijk. Evaluatie en implementatie, respectievelijk fasen drie en vier van het MRC-raamwerk, vallen buiten het bestek van deze dissertatie, maar komen wel aan bod in de algemene discussie van dit proefschrift (hoofdstuk 7).

**Hoofdstuk 2** beschrijft de ervaringen met spasticiteit van mensen met een pure vorm van HSP middels kwalitatief onderzoek. De thematische analyse van de ervaringen gerapporteerd in 14 interviews leidde tot vier thema's: "Ik struikel", "Ik worstel", "Ik schaam me", en "Ik heb ondersteuning nodig". Bij "Ik struikel" worden de ervaren pijn, stijfheid, vermoeidheid, verminderde balans- en loopvaardigheid, en de dagelijkse fluctuaties genoemd. Bij "Ik worstel" gaat het over pogingen om zich aan te passen aan de functionele gevolgen van spasticiteit. Bij "Ik schaam mij" gaat het over de gevoelens van angst en frustratie, en de aanname 'veroordeeld te worden' door anderen. Het thema "Ik heb ondersteuning nodig" beschrijft de wens tot adequate informatie over behandelingen, het vinden van competente zorgprofessionals, en het inzicht krijgen in het beloop van de aandoening en de dagelijkse fluctuaties in de spasticiteit. Ook identificeerden wij diverse (niet-)motorische aspecten van spasticiteit die een grote invloed bleken te hebben op het dagelijks leven. Naast het delen van ervaringen rapporteerden deelnemers problemen met het zich aanpassen aan de gevolgen van spasticiteit en vroegen hiervoor informatie, coaching en ondersteuning.

**Hoofdstuk 3** beschrijft een online survey waarin wij de ervaren klachten en beperkingen in activiteiten en motorische vaardigheden kwantificeerden in een groep van 109 mensen met een pure vorm van HSP. Daarnaast werden karakteristieken onderzocht die geassocieerd worden met loopvaardigheid en valrisico. De deelnemers aan de survey benoemden diverse stoornissen en beperkingen. Naast de bekende motorische symptomen van spasticiteit, zoals spierkramp en spierstijfheid, gaven de deelnemers aan dat niet-motorische symptomen zoals pijn, vermoeidheid, en angst om te vallen grote

problemen vormen in hun dagelijkse leven. Deze niet-motorische symptomen zouden eveneens gemonitord moeten worden. Verder bleek uit statistische analyse de valkans toe te nemen bij personen die: langer last hadden van spasticiteit; niet-neurologische comorbiditeit hadden; en een rolstoel gebruikten. Een soortgelijke statistische analyse liet zien dat personen met een hogere leeftijd, ervaren loopproblemen, en een onvermogen tot 10 minuten kunnen staan of een zware deur te openen, een kleinere kans hadden om zonder loophulpmiddel te kunnen lopen.

**Hoofdstuk 4** gebruikt beschrijvende statistiek om de kwantitatieve data van de hierboven beschreven survey in kaart te brengen met betrekking tot zorgvragen, verwachtingen, zorggebruik, en ervaren behandelresultaten. De zorgvragen van de respondenten betroffen de behandeling van zowel motorische als niet-motorische gevolgen van spasticiteit. Deelnemers verwachtten de grootste behandelresultaten op het gebied van het lopen. Slechts weinigen verwachtten effect op niet-motorische gevolgen van spasticiteit. Revalidatieartsen en fysiotherapeuten waren het meest frequent betrokken bij de behandeling van spasticiteit. Ongeveer een derde van de deelnemers had nog nooit medicijnen tegen spasticiteit gebruikt. Het ervaren effect van medicamenteuze behandeling lag in het verminderen van spasticiteit en het verbeteren van de algehele fysieke fitheid. De overige ervaren effecten verschilden per type medicamenteuze behandeling. Opvallend was de lage behoefte van de patiënt t.a.v. aandacht voor de niet-motorische gevolgen van spasticiteit tijdens het spreekuur van de arts, ondanks dat deze een grote ziektebelasting veroorzaken. Tevens bleek dat de verwachte behandelresultaten gericht op het verhogen van het zelfvertrouwen, verminderen van pijn, en verbeteren van de nachtrust laag was bij de onderzochte groep.

**Hoofdstuk 5** beschrijft de ervaringen met spasticiteit bij 14 mensen na een beroerte, alsmede hun ervaringen met botulinetoxine injecties ter vermindering van spasticiteit. Uit onze analyse van de kwalitatieve data kwamen de volgende drie thema's naar voren: "Spasticiteit-gerelateerde fysieke stoornissen en beperkingen", "Botulinetoxine-gerelateerde fluctuaties in spasticiteit", en "Behoeftes aan professionele ondersteuning en feedback". Bij het thema "Spasticiteit-gerelateerde fysieke stoornissen en beperkingen" vertelden mensen met een beroerte over hun ervaringen met spierstijfheid, abnormale houding, pijn en andere sensaties, verminderde motorische controle, vermoeidheid, schaamtegevoelens, en verminderde sociale participatie. Bij "Botulinetoxine-gerelateerde fluctuaties in spasticiteit" beschreven de deelnemers hun ervaringen gedurende de cycli van botulinetoxine injecties. Bij het thema "Behoeftes aan professionele ondersteuning en feedback" kwam hun wens naar voren met betrekking tot adequate informatie, gedeelde verantwoordelijkheid in de behandelkeuze, optimalisatie van de timing van de injecties, en feedback om beter om te kunnen gaan met spasticiteit. Mensen met een beroerte ervaarden vergelijkbare stoornissen en beperkingen als mensen met HSP en een

vergelijkbare impact op het dagelijks leven. Opvallend was dat ook de deelnemers van dit onderzoek om informatie, coaching en ondersteuning vroegen, net als de deelnemers met HSP aan eerder onderzoek. Mensen met een beroerte vroegen verder om samenwerking met hun zorgverleners in de vorm van gezamenlijk beslissen over de behandelkeuze en de timing van de injecties.

**Hoofdstuk 6** beschrijft de kwantitatieve en kwalitatieve resultaten van een studie naar de haalbaarheid en bruikbaarheid van de ontwikkelde online monitoring tool bij 24 personen met een beroerte, 19 personen met HSP, acht revalidatieartsen, en 27 eerstelijnsfysiotherapeuten. Het percentage patiënten dat bereid was deel te nemen, de mate waarin de patiënten de tool bleven gebruiken, en de bruikbaarheid van de tool werden met behulp van beschrijvende statistiek in kaart gebracht. De bereidheid tot deelname en het voortzetten van gebruik van de tool was groter bij mensen met HSP dan bij mensen met een beroerte. Revalidatieartsen vonden de bruikbaarheid van de tool “marginaal”, terwijl de deelnemers met spasticiteit en de fysiotherapeuten een “goed” scoorden.

Uit de kwalitatieve analyse van de interviews bleek dat online monitoring van spasticiteit-gerelateerde problemen verbeterd kon worden door het monitoren aan te passen aan de persoonlijke wensen en mogelijkheden van de patiënt, en door het inpassen binnen de dagelijks routine van zorgverleners. Ondanks de overeenkomstige wensen met betrekking tot monitoring, zoals beschreven in hoofdstukken 2 en 5, waren er verschillen in de mate van deelname en gebruik van de tool tussen de beide patiëntengroepen. De manier van monitoren en de ervaren voordelen verschilden tussen beide groepen. Sommige personen met spasticiteit vonden dat de tool de spasticiteitsbehandeling ondersteunde, terwijl anderen niet geconfronteerd wilden worden met hun stoornissen en beperkingen tijdens het dagelijks invullen van de tool.

**Hoofdstuk 7** bundelt en ordent de resultaten uit bovenstaande studies tot drie overkoepelende thema's: “Componenten van monitoring”, “Maatwerk in monitoring”, en “Waarde van monitoring”. “**Componenten van monitoring**” beschrijft het belang van het monitoren van door de patiënt gerapporteerde uitkomstmaten die zich niet alleen richten op de klassieke motorische symptomen zoals spierstijfheid, maar ook op niet-motorische symptomen zoals vermoeidheid en pijn. “**Maatwerking in monitoring**” geeft het belang weer van adequate selectie van patiënten voor online monitoring en de timing en intensiteit ervan. “**Waarde van monitoring**” bespreekt de gezamenlijke besluitvorming binnen de totale behandeling van spasticiteit, hoe hierbij rekening gehouden kan worden met de (digitale) gezondheidsvaardigheden van de patiënt, en hoe de zorgprofessional ondersteund kan worden bij het online monitoren van spasticiteit-gerelateerde problemen.

Concluderend wordt gesteld dat het online monitoren van spasticiteit-gerelateerde problemen bij mensen met HSP en beroerte in potentie haalbaar is en dat monitoring het inzicht in het individuele beloop - en derhalve de behandeling - van spasticiteit kan ondersteunen, indien voldoende rekening wordt gehouden met belemmerende en bevorderende factoren.



## List of publications

**Kerstens, Hans C.J.W.**, Nijkrake, Maarten J., De Swart, Bert J.M., Nijhuis-van der Sanden, Maria W.G., Vos- van der Hulst M., Bos, G.J., Geurts, Alexander C.H., Van der Wees P.J. (2022) Online monitoring of focal spasticity treatment with botulinum toxin in people with chronic stroke or hereditary spastic paraplegia: a feasibility study, Submitted

**Kerstens, H.C.J.W.**, Van Lith BJH, Nijkrake MJ, De Swart BJM, Van den Bemd LAC, Smeets RJEM, Fheodoroff K, Van de Warrenburg BPC, Van der Wees PJ, Geurts ACH Healthcare needs, expectations, utilization, and experienced treatment effects in patients with hereditary spastic paraplegia: a web-based survey in the Netherlands. *Orphanet J Rare Dis* **16**, 283 (2021). DOI:10.1186/s13023-021-01915-0

van Lith, B.J.H., **Kerstens, H.C.J.W.**, van den Bemd LAC, der Sanden MWGN, Weerdesteyn V, Smeets RJEM, Fheodoroff K, van de Warrenburg BPC, Geurts ACH. Experienced complaints, activity limitations and loss of motor capacities in patients with pure hereditary spastic paraplegia: a web-based survey in the Netherlands. *Orphanet J Rare Dis* **15**, 64 (2020), DOI: 10.1186/s13023-020-1338-4

**Hans C. J. W. Kerstens**, Ton Satink, Maarten J. Nijkrake, Bert J. M. De Swart, Maria W. G. Nijhuis-van der Sanden, Philip J. Van der Wees & Alexander C. H. Geurts (2020) Experienced consequences of spasticity and effects of botulinum toxin injections: a qualitative study amongst patients with disabling spasticity after stroke, *Disability and Rehabilitation*, DOI: 10.1080/09638288.2020.1746843

**Hans C. J. W. Kerstens**, Ton Satink, Maarten J. Nijkrake, Bert J. M. De Swart, Bas J. H. Van Lith, Alexander C. H. Geurts & Maria W. G. Nijhuis-van der Sanden (2019) Stumbling, struggling, and shame due to spasticity: a qualitative study of adult persons with hereditary spastic paraplegia, *Disability and Rehabilitation*, DOI: 10.1080/09638288.2019.1610084

Ijspeert J, **Kerstens HCJW**, Janssen RMJ, Geurts ACH, van Alfen N, Groothuis JT. Validity and reliability of serratus anterior hand held dynamometry. *BMC Musculoskelet Disord*. 2019 Aug 7;20(1):360. doi: 10.1186/s12891-019-2741-7. Erratum in: *BMC Musculoskelet Disord*. 2019 Sep 17;20(1):433. PMID: 31391035; PMCID: PMC6686461.







## Curriculum vitae

Hans C.J.W. Kerstens was born in Zoetermeer, the Netherlands, on the 22<sup>nd</sup> of February 1970. After finishing secondary school in 1988, he started studying physiotherapy at the Hogeschool Enschede, the Netherlands. After his graduation in summer 1992, Hans started working as a physiotherapist in several primary care practices in the Netherlands and Germany.

In 1993, Hans emigrated to Switzerland where he started working as a physiotherapist in Kreisspital Ruti. Later, in 1997, he went to Schwerpunktspital Uster. During this period in Switzerland, he gained interest in Neurology, Stroke, and spasticity. Consequently, he followed many courses in both the assessment and treatment of persons with neurological impairments. In October 1997, Hans returned to the Netherlands where he accepted a job as a physiotherapist at Rehabilitation Center Blixembosch in Eindhoven. In Blixembosch, his focus shifted even more to Stroke and spasticity. Since Hans became a tutor in neurorehabilitation courses in 2000, he was involved in more than 34 courses in which he taught allied health professionals and nursing staff in the assessment and treatment of patients with Stroke. He gave courses in the Netherlands, Germany, Switzerland, Ethiopia, Singapore, and Denmark. The increasing amount of available evidence for allied health and the collaboration with scientists during these courses, triggered Hans his interest in scientific research. He decided to start the Master of Science in Physical Activity and Health: Biology of Human Performance and Health at the Maastricht University, the Netherlands. After receiving his MSc degree in 2012, Hans accepted a position as lecturer at the school of Physiotherapy of the HAN University of Applied Sciences in Nijmegen, the Netherlands in 2013. Here, he took part in 'de Koppelstructuur', a collaboration between HAN University of Applied Sciences and Radboud University Medical Center that aimed at strengthening meaningful connections in the triangle of education, research, and practice. This boundary crossing activity resulted in a PhD position of which the results are reported in this dissertation.

Currently, Hans still works as a lecturer at the HAN University of Applied Sciences (Minor and Master Neurorehabilitation). Recently, he became both program manager of the Center of Expertise Sneller Herstel, and innovator at Rehabilitation center Klimmendaal and Siza, both in Arnhem the Netherlands in 2021. He is also still involved in the Neurorehabilitation-Stroke course of the Dutch Institute of Allied Health Care (NPi).



## PhD portfolio of Hans C.J.W. Kerstens

Department: **Rehabilitation**  
 Graduate School: **Radboud Institute for Health Sciences**  
 PhD period: **01/09/2016 – 01/07/2022**  
 Promotors: **Prof. dr. P.J. van der Wees, Prof. dr. A.C.H. Geurts**  
 Copromotors: **Dr M.J. Nijkrake, Dr. B.J.M. de Swart**

<b>Training activities</b>	<b>Hours</b>
<b>Courses</b>	
Basiskwalificatie didactische bekwaamheid (2014)	300.00
RU - Qualitative Research Methods and Analysis (2015)	84.00
RU - Effective Writing Strategies (2015)	75.00
Intervention Mapping (2016)	62.00
BKE (2016)	21.00
Kwalitatieve analyse (2016)	16.00
RU - Scientific Writing for PhD candidates (2017)	84.00
Perfecting your academic writing skills (2017)	42.00
Endnote	2.00
Radboudumc - Scientific integrity (2018)	20.00
Radboudumc - eBROK course (2018)	26.00
RU - The Art of Presenting Science (2018)	36.00
RU - Science Journalism and Communication (2019)	80.00
Design thinking and innovation	16.00
<b>Seminars</b>	
Poster presentation HSP patient congress (2016, 2019)	2.00
Oral presentation symposium 'Mobiliteitspoli Radboudumc'	2.00
Oral presentation HSP patient congress (2022)	1.00
Oral presentation Scientific meeting on patient centeredness in spasticity rehabilitation (2016)	2.00
<b>Conferences</b>	
Poster presentation NNR congress (2016)	2.00
<b>Other</b>	
Presentation Summercourse Neurorehabilitation Singapore (2018)	10.00
Presentation Summercourse Neurorehabilitation Copenhagen (2019)	10.00
Presentation Neurorehabilitation -Stroke courses NPi (2020 – 2021)	30.00
<b>Teaching activities</b>	
<b>Lecturing</b>	
Lecturing minor Neurorehabilitation HAN (2016 – 2021)	300.00
<b>Supervision of internships</b>	
Supervision of internships Bachelor students Physiotherapy (2016 – 2021)	240.00
<b>Total</b>	<b>1463.00</b>



## Research Data Management

For each study of this PhD dissertation, the research proposal was submitted to the Medical Ethical Committee for approval. All studies were performed following the principles of Good Clinical Practice, the Netherlands Code of Conduct for Research Integrity, and the Declaration of Helsinki.

The obtained data have been stored in the Radboud University Medical Center on the secured disk 'Q:\Research\104 Me and my cloud'. The folders at this location are numbered in accordance with the chapters of this dissertation, and contain the raw data, the documents for the medical ethical committee, and the final version of the manuscripts. The data is accessible only by the main researcher and the secretary of the Rehabilitation department of the Radboud University Medical Center.

The obtained data will be stored for 5 years after termination of each specific study. The participants did not give informed consent for public use of the data, or for use other than the aim of the particular study. Therefore, re-use of the data of the studies is only possible after a renewed informed consent of the participants.



## Dankwoord

Het leven van een promovendus kent vele pieken en dalen. En ook ik heb een aanzienlijke mate van stuurmanskunst nodig gehad om de diverse belemmerende en bevorderende factoren vanuit het dagelijkse werk, de promotiewerkzaamheden en de persoonlijke omstandigheden te kunnen managen. Het was de afgelopen jaren niet bepaald 'neap tide' oftewel doortijd voor mij. Ik heb hulp gehad van diverse mensen om koers houden. Ik ben dankbaar voor de bijdrages van al deze mensen gedurende mijn reis. Een reis waarin ik zowel als mens als ook als professional enorm ben gegroeid. Ik zou het zo weer over doen, en soms vraag ik mij zelfs af, waarom heb ik deze reis niet eerder mogen maken?

Ik heb mijn promotieonderzoek altijd beschouwd als een nalatenschap aan de maatschappij. Mijn eigen kleine bijdrage aan het creëren van een betere wereld en het verbeteren van de kwaliteit van zorg. Daarom wil ik als eerste mijn dank uitbrengen aan alle patiënten en zorgprofessionals die deelgenomen hebben aan de voorbereidingen en daadwerkelijke uitvoering van de studies. Hoe belangrijk deze samenwerking is, en hoe lang de weg is die wij mondiaal nog moeten gaan, realiseerde ik mij pas echt toen ik de feedback las waarin een reviewer van een van de studies stelde dat '.....filling out this questionnaire by patients without familiarity with medical expertise is not meaningful'. Er is nog een lange weg te gaan voordat persoonsgerichte zorg echt op de kaart gezet is.

Ik besef mij terdege wat voor een fantastisch promotieteam ik om mij heen heb. Een team dat mij niet alleen begeleidde in mijn ontwikkeling als professional, maar mij ook op persoonlijk vlak belangrijke lessen heeft geleerd en soms zelfs een reddingsboei toewierp. Philip, jij stapte wat later aan boord, en nam de plaats van Ria in. Voor mij was dat een spannend moment omdat ik niet kon voorspellen hoe deze wisseling uit zou pakken op de koers van het onderzoek en de samenwerking binnen het bestaande team. Gelukkig bleek al heel snel dat je een enorme aanvulling was. Je hebt een prettige en directe wijze van coachen en begeleiden, je feedback is snel, helder en gestructureerd. Een fijne steun in de rug. Dank ook voor de prettige samenwerking in bijvoorbeeld het aanvragen van subsidie en het brainstormen over de focus van mijn carrière na het promotietraject. Sander, wij kennen elkaar sinds 2000 door jouw gastlessen balans tijdens neuro-cursussen. Dat waren altijd inspirerende uren, hetgeen versterkt werd tijdens de samenwerking in het ontwikkelen en uitvoeren van de cursussen Neurorevalidatie-CVA van het NPi. Je bent voor mij een voorbeeld in het combineren van klinische expertise en wetenschappelijke evidentie. Fijn dat jij mij als promotor daarvan liet leren en profiteren. Je stond aan de basis van mijn promotietraject. Letterlijk, door je ideeën over het ontwikkelen van een monitoringsysteem en de financiële bijdrages die je wist te verwerven voor het ontwikkelen en onderhouden van het systeem. Maar bijvoorbeeld ook door de pittige gesprekken met de commerciële partijen waarmee je mij ondersteunde in het vlot trekken van het

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